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THE MECHANISM AND PHYSIOLOGY OF SEX DETERMINATION

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THE MECHANISM AND PHYSIOLOGY OF SEX DETERMINATION

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TRANSLATOR'S PREFACE

THIS translation of Professor Goldschmidt's work on the Physiology and Mechanism of Sex Determination is offered as an attempt to present to English-speaking students a summary of the more recent investigations on a problem of the greatest interest to biologists, medical men, breeders, and indeed the general public. The manuscript was submitted to Professor Goldschmidt, who made additions and changes bringing the subject-matter up to more recent date than the German edition.

Scientific investigation in the field of sex determination and heredity is now being pursued with great vigour in many countries, and there is every prospect of great success in the future in the elucidation and probably the actual control of sex.

The German edition of the work was dedicated by Goldschmidt to Professor Richard Hertwig. If it were possible for me to dedicate the English translation it would be to the memory of the late Professor Leonard Doncaster, whose classic work is so often referred to within its pages, and whose untimely death robbed us of one whose name will always be associated with the problem of the inheritance and determination of sex.

WILLIAM J. DAKIN

LIVERPOOL
July, 1923

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IX

THE MECHANISM AND PHYSIOLOGY OF SEX DETERMINATION

THE MECHANISM AND PHYSIOLOGY OF SEX DETERMINATION

SECTION I

CHAPTER I

INTRODUCTION. THE NATURE OF SEX

THE majority of biological sex problems—and of these only is there any discussion in this book—arise from the presence of two different sexes in the realm of living organisms. The problems resulting from this (and their solution) constitute one of the most fascinating chapters of the science of life. In addition it is one which has responded most successfully to investigation, both in regard to the richness of the results and the depth of penetration in the direction of a causal and physiological understanding. The greater part of the following work is devoted to a presentation of these problems, but it must not be forgotten that this is not the whole of the problem of sex. The presupposition for the distinction of sexes is of course the presence of sexual reproduction. This is regarded as one of the fundamental problems of Biology, the solution of which would remove the veil from a great part of the secret of life. The moment for this has not yet arrived, but a proper consideration of the material which has now accumulated from countless experiments and observations gives some idea of the direction in which we may look for the complete solution.

It is not so long ago that entire groups of organisms were held to be of such simple organization that they were only capable of reproduction by simple binary fission. With increasing knowledge the number of such organisms has gradually diminished, and now in the animal world (and in the following chapters we are concerned only with this section of living organisms) there is scarcely an example of which we can say with certainty that its only means of reproduction is asexual. Early or late, there comes, for all animal organisms, a moment when a sexual act of some kind takes place. As a rule it is some process of fertilization, a junction or fusion of male and female elements. In other cases, however, it is parthenogenesis—a sexual act without the participation of a male element. In the first place, therefore, sex must be considered independently of fertilization; it is an elementary phenomenon to which the process of fertilization is secondarily appended. The chief problem may then be stated as follows: "Why does the animal organism (even the simplest) require the regular repetition of sexual processes in order to continue its racial existence?" Expressed in another form: *multiplication* and *reproduction* is doubtless a form of growth beyond the limits of the individual through and by which successive generations are materially continuous with each other. Why then is a permanent growth impossible unless the interpolation of a sexual process gives a fresh start or impetus to it?

These questions indicate that the roots of the problem of sex are bound up with the problems of age, death, and immortality. They have all received consideration in the investigations and speculations of modern Biology, and we need only mention the names of Bütschli, Hertwig, Maupas, Weismann and the catchwords, "Rejuvenescence" and "Amphimixis," which are familiar to all biologists.[1] But we will not discuss the numerous more or less formal theories which have been put forward at different periods, but present the chief facts in such a way that we may see the direction in which a solution is to be looked for.

In the Metazoa, reproduction is effected by the sex or germ cells, egg cells which develop parthenogenetically or are fertilized by sperm cells. These cells form the continuous material bridge between the generations, they are links in a continuity which is theoretically unlimited—in this sense they are im-mortal. The rest of the organism commences its existence with the separation of the somatic cells from the germ cells and terminates with death. The physiological significance of this is that the cells of the body become exhausted through their functioning, and finally their existence as living cells must come to an end. In what way this is brought about does not concern us here. The fact, however, is clear.

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[1] Bütschli, O., "Untersuchungen über die ersten Entwicklungsvorgänge," etc. Frankfurt, 1876.—Weismann, A., "Über Leben und Tod." Jena, 1882.—Maupas, E., "Recherches expérimentales sur la multiplication des infusoires ciliés." Arch. Zool. exp. gén., 6, 1888.—Minot, Ch. S., "The Problem of Age, Growth, and Death." London, 1908.—Hertwig, R., "Über den Ursprung des Todes." Beilage zur Allgem. Ztg., 1906.—Hartmann, M., "Tod und Fortpflanzung." Munich, 1906.—Doflein, F., "Das Unsterblichkeitsproblem im Tierreich." Freiburg, 1913.—Loeb, J., "The Organism as a Whole." New York, 1916.—Child, E. M., "Senescence and Rejuvenescence." Chicago, 1915.—Lipschitz, A., "Allgemeine Physiologie des Todes." Braunschweig, 1915.—Korschelt, E., "Lebensdauer, Alter und Tod." Jena, 1917.

Thus the chief feature of the reproductive or sex cells, contrasted with the cells of the rest of the body, is that they are not being used up physiologically during the life of the individual. The somatic cells—muscle, nerve, and gland cells, for example—functioning for the whole body, carry out work which through chemical limitations necessarily leads to death. The sex cells remain protected from these malignant functions, they rest—*sit venia verbo*—physiologically virginal, and are in a position therefore to survive the rest of the body in their descendants. For this reason the position of the sex cells in the body has often been compared to that of a parasite—not altogether a happy comparison. A better, perhaps, would be with the queen in a Termite colony; she, whilst taking no active part in the working life of the colony, is supported by the workers, for the sole purpose of reproducing the following generations. This peculiar position of the sex cells in the body is revealed in their history. One of the most striking facts of animal embryology is the early separation of the germ cells; it can be demonstrated in all the groups. The number of exceptions steadily diminishes and these

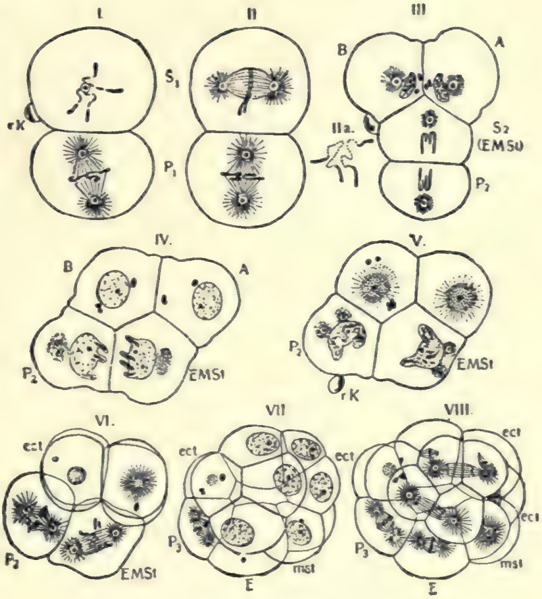

FIG. 1.—Eight segmentation stages of *Ascaris megalocephala*, demonstrating chromatin diminution.

S_1, the primordial somatic cell; P_1-P_3, the stem cells of the germ cells; S_2, the second primordial somatic cell; E_1, ect Ectoderm anlage; mst. Anlage of Mesoderm and Stomodaeum; rk. polar body; IIa, the chromosomes of the primitive somatic cell. After Boveri from Harms.

will probably disappear altogether. For the purpose of illustration we will give two typical cases. The classical example (discovered by Boveri[1]) is the lineage of the germ cells of *Ascaris* (Fig. 2).

The first division of the *Ascaris* egg gives two cells which can be recognized from the beginning as constitutionally different in regard to their nuclei. From one, part of the chromatin is lost, while the other suffers no diminution. The former cell by division gives rise exclusively to somatic cells, ectodermal cells (see illustration, Fig. 2). The second fission of the egg divides the other cell into two. Of these one cell undergoes similar nuclear changes resulting in chromatin diminution and is destined in the succeeding divisions to give rise only to somatic cells. The third, fourth, and fifth divisions are similar, each time one cell being destined to produce only somatic cells.

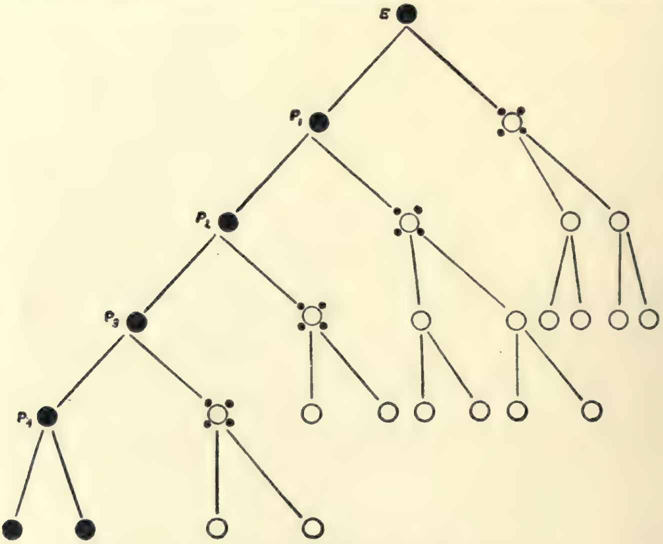

FIG. 2.—Diagram of the cell lineage in the *Ascaris*. Black denotes the Keimbahn; white the diminished somatic cells.

After Boveri.

Finally, the non-diminishing cell divides into two—the two primitive sex cells—and these can be recognized quite distinctly in the embryo. All the sex cells of the adult are developed from these two original cells and they number some millions. The Keimbahn (germ tract) is clearly visible therefore from the fertilized egg to the germ cells of the next generation.

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[1] Boveri, Th., "Die Entwicklung von Ascaris megalocephala," etc. Festschr. f. C. v. Kupffer, 1899.

No less instructive is the example of the parthenogenetic gall fly *Miastor* (Kahle. Hegner) illustrated in Fig. 3. Even in the undeveloped egg a difference in the protoplasm can be detected at one pole (polarplasma p. pl.). After the extrusion of the polar bodies segmentation begins, but, as is typical of the Arthropoda, no cell boundaries are formed. When the stage with four nuclei is reached we are reminded of the conditions in *Ascaris.* Three of the nuclei suffer a diminution of chromatin in their further divisions; the fourth divides without such diminution, and one of the daughter nuclei comes to lie in the polarplasma (Fig. 3, b) which separates itself off from the rest of the egg and becomes the primitive germ cell (Fig. 3, c). The other nuclei with the rest of the protoplasm give rise to the organs of the embryo in the manner typical for the Insecta. Meanwhile the primitive germ cell divides into four (Fig. 3, d.), and by further division eight cells result which arrange themselves in the young embryo to form an ovary (Fig. 3, e). This is the complete cycle of the germ plasm, for out of these primitive sex cells the parthenogenetic eggs of the new generation will arise.

These cases (and there is an abundance of analogous examples [1]) present the following important facts for our general survey. In the first place the material for the constitution of the sex cells is set aside at the commencement of development, a view supported also by experiments in which the cells concerned having been destroyed in early stages of development, the resulting animals showed a complete absence of sex cells (Hegner,[2] Reagan).[3] The material which is thus set aside often presents visible structural peculiarities, for example deposits of special substances in the protoplasm, so-called Keimbahn (germ tract) determinants of which some examples are given in Fig. 4, or peculiarities associated with the chromosomes as in the cases of *Ascaris* and *Miastor* already cited, where there is chromatin diminution. The difference in material can also be experimentally demonstrated as was shown by Boveri in his ingenious work on *Ascaris.*[4]

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[1] Hegner, R. W., "The Germ Cell Cycle in Animals." New York, 1914.

[2] See the summary by Hegner, R. W., *ibid.*

[3] Reagan, F. P., "Some Results and Possibilities of Early Embryonic Castration." Anat. Rec., 11, 1916.

[4] Boveri, Th., "Die Potenzen der Ascarisblastomeren bei veränderter Furchung." Festschr. R. Hertwig. V. 3, 1910.

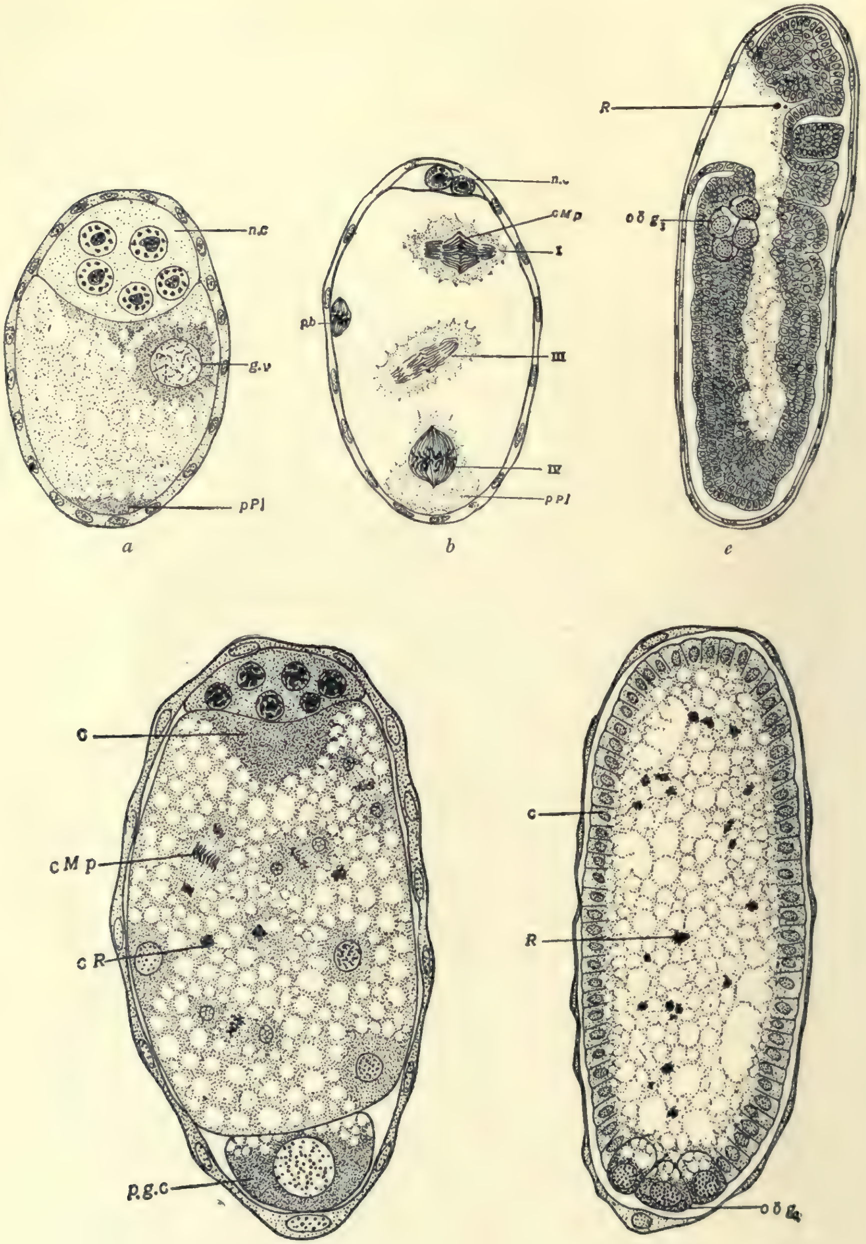
n.c
g.v
pPl
a
n.c
cMp
I
pb
III
IV
pPl
b
R
oög
e
c
cMp
cR
p.g.c
c
c
R
oög
d

FIG. 3.—The Keimbahn of the Gall Fly *Miastor*.

a, the egg with nurse cells nc, the nucleus gv, and the pole plasm pPl; b, the first segmentation stage with three division figures I, III, and IV; pb polar body, cMp the chromatin to be eliminated; c, later segmentation stage; cR chromatin remains, c cytoplasm, pgc one of the germ cells; d, stage after formation of blastoderm c, oög oogonia, R chromatin remains.

These elements so set aside take no active part in the other functions of the body. This has been demonstrated in cases where they can be removed without taking away other cell elements such as the interstitial glands of higher organisms. In such examples a completely normal individual results except for the absence of sex cells (castration experiments of Oudemans, Meisenheimer, Kopec, and Hegner). Further support for these views is supplied by many interesting facts, as for example the cases where quite young caterpillars of Lepidoptera are found with developed testes containing ripe sperm cells, when the rest of the body has still to go through the whole series of physiological phenomena of growth and metamorphosis. The sex cells are therefore from the beginning to the end of their existence freed on behalf of the whole body from the consuming physiological activity of the somatic cells, and their activity is merely such as is proper to their own metabolism.

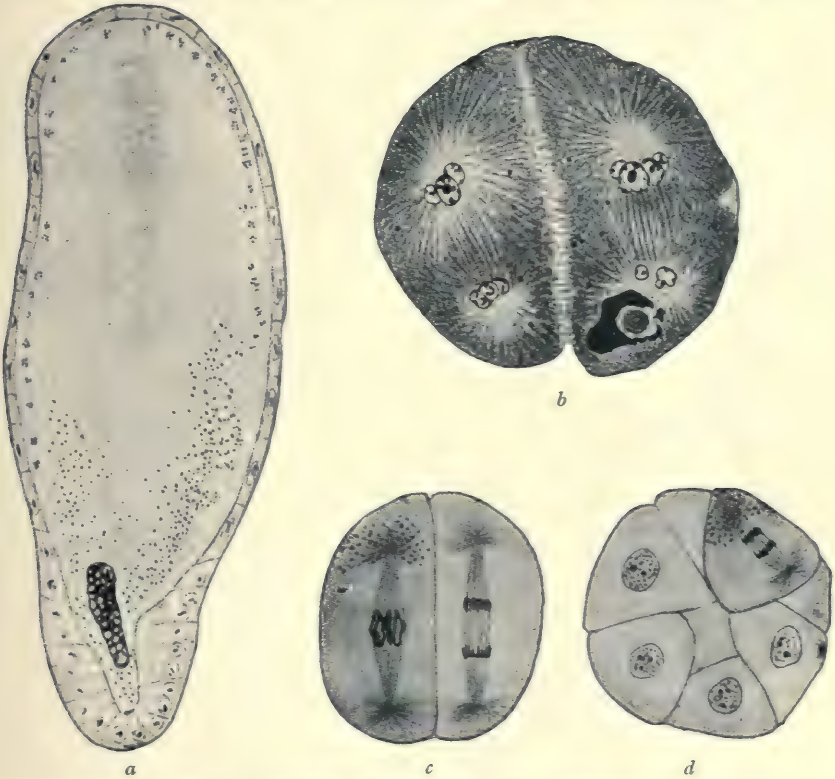

Fig. 4.—Types of Keimbahn determining substances.
a, in the Ichneumon egg (after Buchner); b, in a segmentation stage of Polyphemus (after Kühn); c and d, in segmentation stages of Cyclops (after Amma).

Since the physiological nature of sexual reproduction is something independent of bisexuality, let us for a moment confine our attention to the egg cell which alone should disclose the physiological nature of sexual reproduction. Whilst the sex cells as a whole have a different history from the somatic cells, their individual history exhibits an abundance of diversity. In fact there is a host of peculiarities, a knowledge of which is absolutely essential for the solution and understanding of our problem. The elucidation of the life history of the sex cells comprises the greater part of the cytological work of forty years.

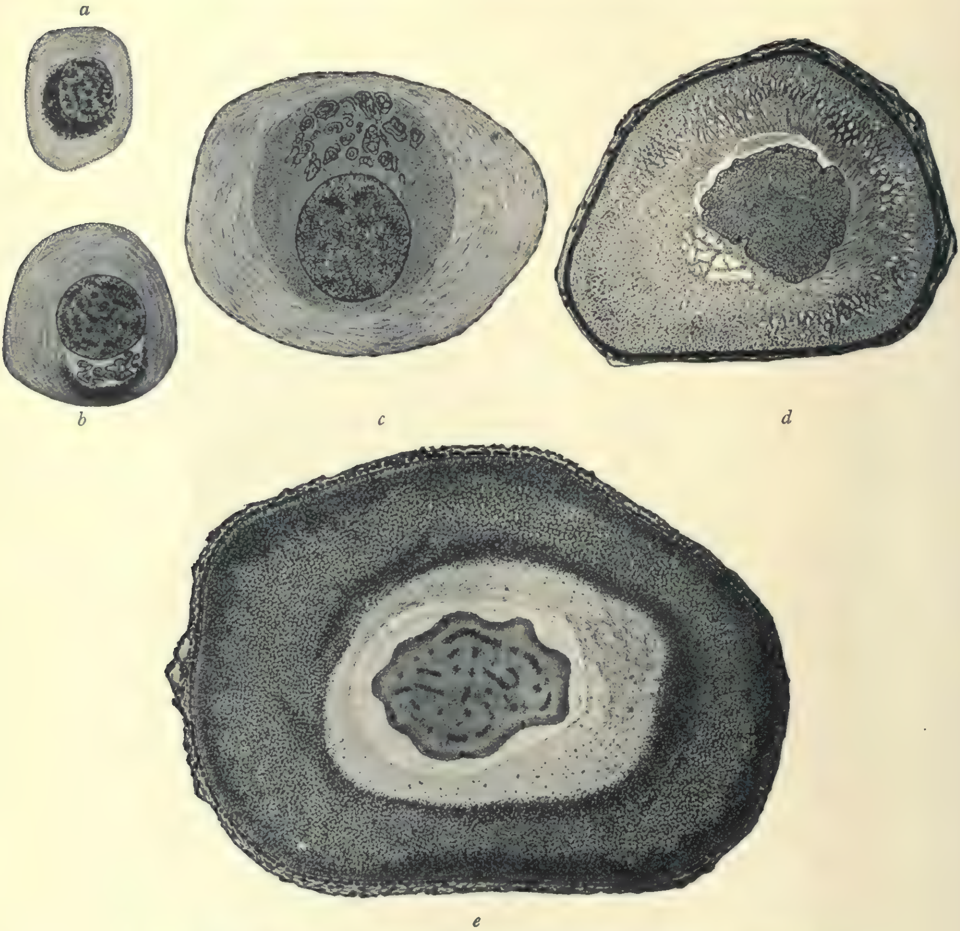

FIG. 5.—Five stages in the oogenesis of *Proteus* demonstrating the changes in the Cytoplasm and Nucleus.

(d and e not so highly magnified as a-c.)

After Jörgensen.

From the vast array of facts let us examine some of those which appear important for the understanding of our special problem.

The peculiarities of the life history of the sex cells commence with a series of complicated phenomena in the nucleus—the synaptic processes (these will be discussed later, their chief importance is associated with other questions). Then, in the case of the egg cell, the period of growth follows, a period of intense physiological activity which is announced by a series of changes in nucleus and cytoplasm. Amphibian and Selachian eggs may be taken as examples. In Fig. 5 a series of stages from one of these growth periods is illustrated; some of the changes are shown, although minute features cannot be depicted without greater magnification. One can see that the protoplasm constantly changes in structure the morphological expression of chemical processes which lead to the storage of yolk and organ-forming substances. Along with these alterations occur changes inside the nucleus which are amongst the most complex phenomena made known by cytological study. The illustration only shows how the growing chromosomes arrange themselves in the most diverse manner in the nucleus. The more highly enlarged Fig. 6, of a Selachian egg, shows how all kinds of bodies, nucleoli, etc., appear in the nucleus only to disappear again, whilst other nuclear structures constantly alter, changes which point to the intense activity within the nucleus. When the growth period has come to an end and the maturation divisions begin, the chromosomes become more clearly visible, but their volume is now only a small fraction of what it was in the growth period (see Fig. 6 h). At the maturation division which now takes place the extremely large nucleus breaks down, the chromosomes only remaining, and in the case of animals like the sea urchin, where the egg nucleus passes through another resting period after maturation, the ripe nucleus is much smaller than the unripe.

Rückert[1] was the first to grasp the real significance of this phenomenon, his conception being further developed later by Lubosch, Goldschmidt, and others.

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[1] Rückert, J., "Zur Entwicklungsgeschichte des Ovarialeies der Selachier." Anat. Anz., 7, 1892.—Goldschmidt, R., "Der Chromidialapparat lebhaft funktionierender Gewebezellen." Zool. Jahrb. (An.) 21, 1904.—Lubosch, W., "Über die Eireifung der Metazoen," etc. Merkel u. Bonnets Ergebr., 11, 1901; 21, 1914. (References to Literature.)—Buchner, P., "Vergleichende Eistudien I." Arch. mikr. An. 91, 1918.

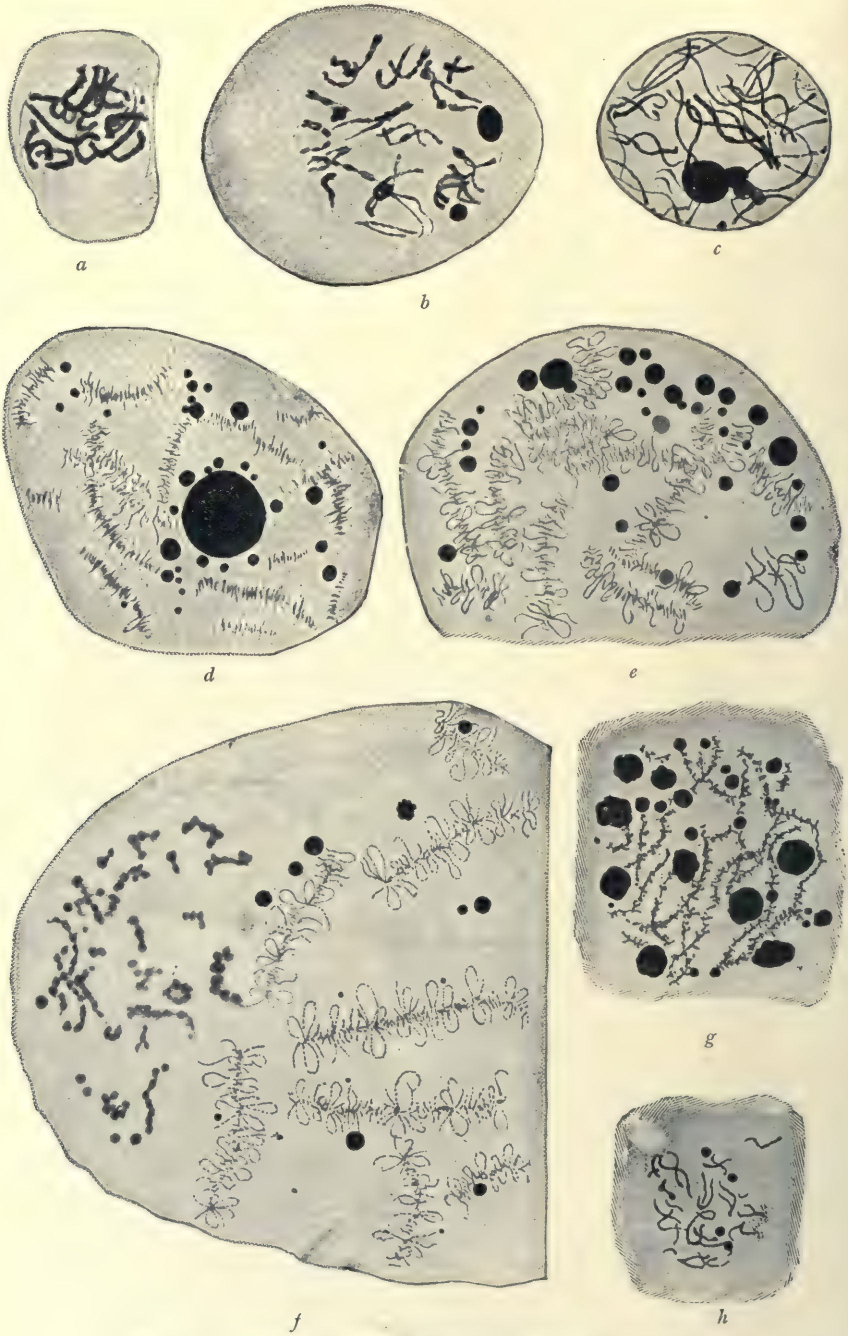

FIG. 6.—Chromosomes and Nucleoli of the growing Selachian egg.
a, pachytene bouquet stage; b-f, unfolding of the brush-like chromosomes; g, h, diminution of the chromosomes before the first maturation division.
After Maréchal from Buchner.

The nuclear substances, especially the chromatin, play an important rôle during the growth period and probably influence in some way the processes taking place in the cytoplasm. From these physiologically active substances the material of the chromosomes separates itself (the two types of chromatin are usually termed Trophochromatin and Idiochromatin) and it passes on alone, and to a certain extent purified or free from metabolic products, to the mature egg.

The result of all these phenomena is a cell which contains in its protoplasm the chemical material necessary for successful development, in its nucleus the chromosomes cleansed physiologically from waste products. This nucleus is now in the same condition physiologically as that which initiated the previous generation.

Following our previous method, if we try to deduce from these facts the information which is most important for our problem, we find that one of the tasks which many egg cells have to perform before being capable of fertilization is the storage of material to provide for the needs of the developing organism, both as a source of energy and as a source of specific and formative building material. The requirement of stored material as a source of energy will of course depend upon the opportunities the embryo has of utilizing external sources of energy, but organ-forming substances are absolutely necessary. They may not often be so clearly visible as in the Ascidian egg (Fig. 7), but their presence has been experimentally demonstrated times without number. We can therefore say in general that one of the conditions for the fulfilment of the function of the egg cell is the collection and storage of those organ-forming chemical substances which enable the developing organism to construct its specific tissue material out of its internal and external food supplies. What these are chemically we do not know with certainty. They include all those substances which are commonly regarded as the material basis of heredity, and possibly in addition an assortment of "materials" which form the basis for the specificity of synthetic products during development.

The general nature of sexuality in the Metazoa may therefore be characterized as follows: Early segregation of cells which are freed from those functions of the body which for physico-chemical reasons necessarily lead to death; preparation of these cells for their special function of producing organisms like the parent, by the storage of material as a source of energy, by the deposition of substances in the cell body which are necessary for the specific constructive processes of development, and by the cleansing of the nucleus from all but the complex of substances bound up with the chromosomes and associated with heredity.

This discussion has taken for granted the fact that the body cells sooner or later must for chemical reasons terminate in death. Although our daily biological experience teaches that this is correct, yet we desire the possibility of experimental proof of the same. The only chance of providing such is by the investigation of Metazoa which reproduce asexually as well as sexually. Experiments of this kind have been carried out on the fresh-water polyp *Hydra*, especially by R. Hertwig and his pupils,[1] and also more recently by M. Hartmann on the Turbellarian, *Stenostomum*.[2] In spite of many interesting facts no decisive results approaching in clarity those derived from a study of the Infusoria have been reached on this point. Atten-

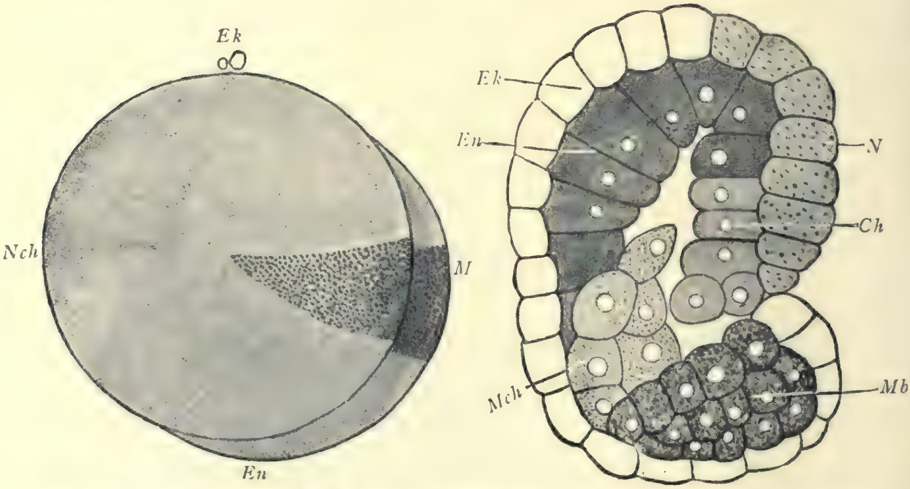

FIG. 7.—Egg and Embryo of the Ascidian *Cynthia* for demonstration of the organ-building substances

Ek, Ectoderm or protoplasmic Anlage of the same; Nch, Anlage of the Neurochord; N, Nervous system; Ch, Chorda; En, Entoderm; M, common Anlage for Mesenchyme (Mch) and Myoblasts (Mb). After Conklin from Buchner.

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[1] Hertwig, R., "Über Knospung und Geschlechtsentwicklung von Hydra fusca." Biol. Centrbl., 26, 1906.—Krapfenbauer, E., "Einwirkung der Existenzbedingungen auf die Knospung von Hydra." Diss. Munich, 1908.—Frischolz, E., "Zur Biologie von Hydra." Biol. Centrbl., 29, 1909.

[2] Hartmann, M., "Über den dauernden Ersatz der ungeschlechtichen Fortpflanzung durch fortgesetzte Regeneration." Biol. Centralbl., 42, 1922.

tion has been drawn to such organisms as those which pass the winter in resting stages (as, for example, the gemmules of the fresh-water sponge and the statoblasts of Bryozoa). We do not know, however, whether the production of these resting stages is not accompanied by phenomena equivalent physiologically to the sexual processes, nor do we know how often these asexual acts can be repeated without interpolated sexual phenomena. One might point to certain cases of regeneration, as, for example, the fact that quite small pieces of the Ascidian *Clavellina* will regenerate the entire animal. But the two problems embodied in the sentence above are not solved by this example in which the same result is attained, except that the voluntary action of the sponge and the Polyzoan is replaced by experiment. The conclusions drawn above in regard to sexuality in the Metazoa are therefore probably free from objection.

In the discussion of sexuality the conditions in the Protozoa have always played a prominent part, and as a matter of fact a knowledge of these and a thoroughly critical study of their significance is of the greatest importance. To-day there is no group of the Protozoa in which the absence of sexual processes has been demonstrated, in fact the most important part of modern protozoology deals with the elucidation of sexual cycles. But the details of sex processes in the Protozoa are not so easily described as those of the Metazoa, owing to a diversity so great that a knowledge of the chief types is necessary before we can arrive at a general formulation. We shall therefore glance at a few of these cases.

The reproductive cycle of a Gregarine is taken as the first type because the conditions come nearest to those of the Metazoa. It is depicted diagrammatically in Fig. 8. The sexual act begins with the approximation of two individuals which we can designate as male and female. Round these a common cyst is produced. In each individual the nucleus now forms a spindle, and through successive divisions a large number of nuclei result (a considerable part of the nuclear material of the parent nucleus undergoes destruction altogether). The nuclei produced in this manner migrate to the surface in each individual where each one becomes associated with a small mass of cytoplasm. These nucleated masses are the gametes and often they can be distinguished as male and female, in fact the male gametes may possess a structure rather like that of Metazoan spermatozoa.

The gametes copulate in pairs to form zygotes, and these each develop a cyst so that the original cyst contains a number of encysted zygotes—the spores. Further division still takes place within these, so that each may contain several sporozoites which are in reality young Gregarines ready to develop further upon entrance into the proper host.

Another type of sex is presented by the Foraminifera—it is shown diagrammatically in Fig. 9. Here as in many Protozoa there is an alternation of sexual and asexual reproduction. The asexual individuals are termed the microspheric forms on account of the small innermost chamber. These individuals become multi-nuclear as they develop owing to the fission of the original nucleus. When asexual reproduction takes place the protoplasm collects round these nuclei and a number of small Amœbæ-like progeny leave the maternal organism and proceed to secrete shells of their own. In these, however, the initial chamber is large, a character of this generation when fully grown. It is termed the macrospheric or sexual generation. The initial nucleus of the macrospheric individual eventually separates into two parts, one of which is a vegetative or trophochromatic nucleus whilst the other, a mass of reproduction-chromatin or Idiochromatin, is usually termed a chromidial mass. The latter breaks up into numerous small bodies which finally are recognizable as small nuclei. They surround themselves with proto-

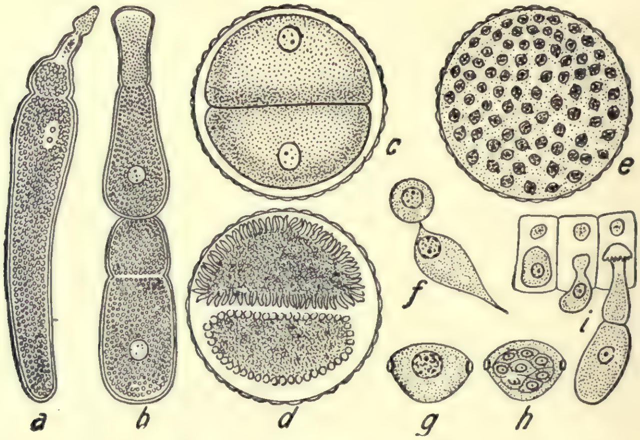

FIG. 8.—Life Cycle of a Gregarine.

a, individual; b, copulation; c, the two individuals encysted; d, spore formation; e, cyst with ripe spores; f, copulation of the gametes; gh, spores with sporozoites; i, growth of the young gregarine in an epithelial cell.

From Selenka-Goldschmidt.

plasm and develop into the gametes. At the beginning of the reproductive period, however, the vegetative nucleus breaks up and disappears whilst the gametes swarm out and copulate in pairs—the individuals of a pair having come from different parents. The zygotes thus formed develop into the microspheric and asexual generation. This completes the life cycle.

A third and again different type of sex as seen in the Protozoa is presented by the Heliozoan, *Actinosphærium* (Fig. 10). In this case a single multinuclear individual becomes encysted for the purpose of sexual reproduction. A large number of the nuclei now degenerate, whilst the others are surrounded by little masses of protoplasm which secrete envelopes—the secondary cysts. In each of these the nucleus and protoplasm divide into two. Each daughter nucleus so formed throws off a "polar body," reminding one of the Metazoan egg cell, and then both nuclei (now mature) fuse together again. The fertilization thus takes place between two sister nuclei which

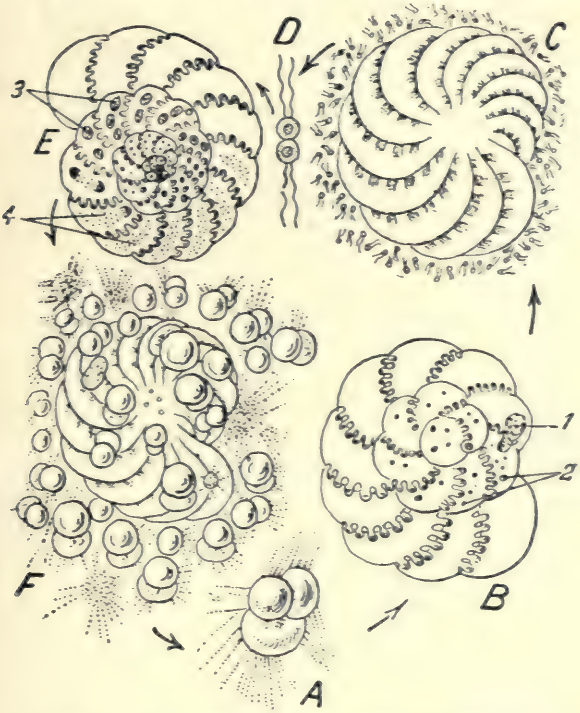

Fig. 9.—Life Cycle of the Foraminiferan *Polystomella*.

A-C, the megalospheric generation; 1. principal nucleus, 2. secondary nuclei, 3. nuclei, 4. chromidia; D copulation of the swarm spores; E, F, the microsphæric generation in asexual reproduction.

From Selenka-Goldschmidt.

have resulted from the division of one and the same nuclear mass. Out of each secondary cyst a little *Actinosphærium* creeps.

Finally, a fourth type of sexuality presented by the Protozoa is the familiar conjugation of the Infusoria (Fig. 11). The Infusoria possess two kinds of nuclei, the macronucleus and one or more micronuclei. In typical conjugation two individuals come together side by side, and whilst the macronucleus begins to break up and disappear, the micronucleus in each individual undergoes certain divisions. Two divisions lead to four nuclei in each *Paramœcium.* Three of these in each case degenerate and may be considered equivalent to polar bodies. The fourth one divides again into two, and of these one remains stationary whilst the other (the migratory nucleus) wanders across into the other individual where it fuses with the stationary nucleus. Each migrating nucleus, therefore, fertilizes the stationary nucleus of the other individual. Following on this the two *Paramœcia* separate and the fertilization nucleus in each organism gives rise by fission to a micronucleus and a macronucleus.

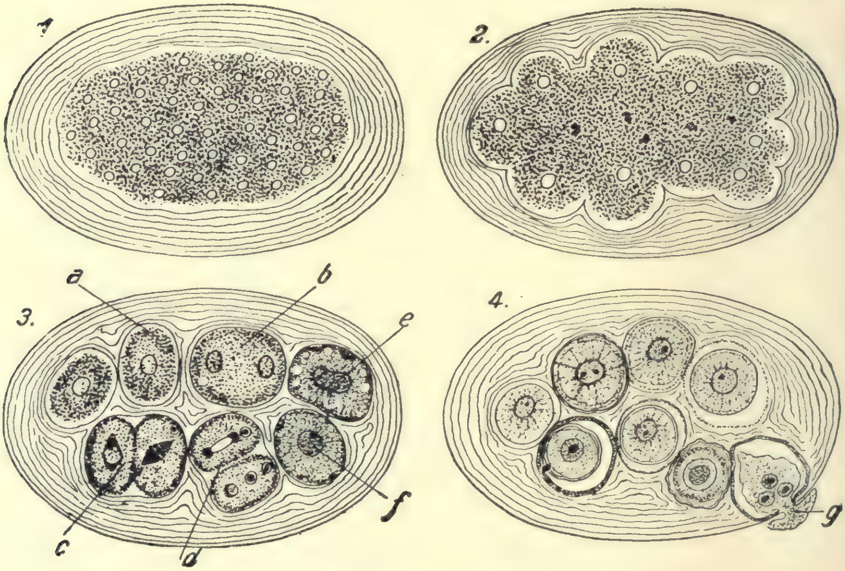

Fig. 10.—Reproduction of *Actinosphærium.*

1, the reproduction cyst; 2, division to form the primary cyst, degeneration of the superfluous nuclei; 3, formation of the primary cysts a, the secondary cysts b, the two maturation divisions c, d, the fertilization e, the zygote f; 4, escape of the young individuals g.

From Selenka-Goldschmidt.

If we would supply the physiological interpretation of these facts in connection with the sex problem, we must try to grasp their general character as we have done for the Metazoa. But in attempting this we come up against overwhelming difficulties arising from the conception of the unicellularity of the Protozoa. Is the Protozoan cell comparable to the body cell of the Metazoan, or the sex cell, or does it vary—being sometimes one, sometimes the other. The solution of this and other difficulties (and hence one of the fundamental problems of Comparative Anatomy) has in our opinion been found by Dobell.[1] Dobell considers that the conception of unicellularity in the Protozoa is wrong; rather should they be termed *non-cellular.*

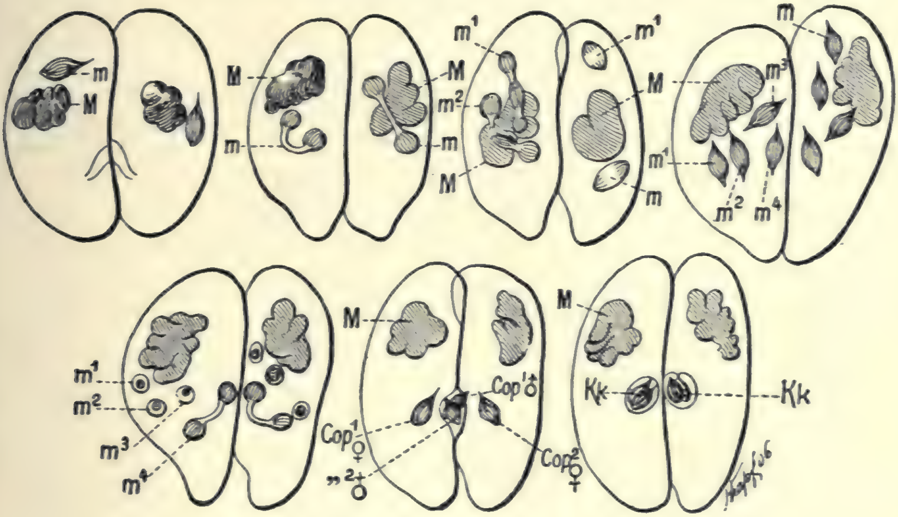

FIG. 11.—Diagram of Conjugation of *Paramæcium.*

M, macronucleus; m, micronucleus; m_1-m_4 parts of the micronucleus; Cop ♂, migratory nucleus; Cop ♀, stationary nucleus; Kk, conjugation nucleus.

From Selenka-Goldschmidt.

In their organization the Metazoa have made use of the method of dividing into cells, the Protozoa have not. The first are therefore cellular, the latter are not. The Protozoan is neither morphologically nor physiologically comparable with any cell of a Metazoan; it is comparable to the whole organism. This conception permits of us drawing comparisons, for it makes it possible to regard the nature of sexuality in the Protozoa from the same point of view as in the Metazoa.

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[1] Dobell, H. C., "The Principles of Protistology." Arch. Protistenk, 23, 1911. Curiously enough Dobell has strongly attacked the views outlined in most general form on these pages although they provide a perfect illustration of his own theory.

We must determine first what there is in the Protozoan which bears the doom of death, something, that is to say, physiologically like the body cells of the Metazoa, and what there is present physiologically like the sex cells of the Metazoa, which untouched by these mortal influences makes it possible to commence life anew. When we regard the reproductive cycles detailed above from this point of view we perceive the following physiological analogies to the Metazoan conditions.

In sexual reproduction in the Protozoa it may be said that a corpse remains which is physiologically comparable to the body cells of the Metazoa. In the case of the Gregarines it is the greater part of the protoplasm and quantitatively the greater part of the nuclear material. The same thing holds good for the Rhizopoda. In *Actinosphærium* it is a certain part of the protoplasm and a considerable amount of nuclear material. In the Infusorian it is the entire macronucleus.

In the Protozoa the material necessary for the formation of the new organism is reserved and kept free from the general metabolism just as is the case with the Metazoan sex cells.

This is not always visible directly, but it can be deduced in all cases. It can be actually seen in those examples where the material for the nuclei of the future gametes is stored as propagatory chromidia in the cytoplasm (Sporetia, Goldschmidt; Idiochromidia, Mesnil) or where it lies already within a nucleus (Hartmann's polyenergid nuclei).[1] It is particularly clear in the Infusoria where the sex nuclear material is separated in the form of one or more micronuclei (the homologues of the propagatory chromidia) during life and from the beginning of the individual existence (like the germ tract (Keimbahn) of *Miastor*), whilst the general body functions are taken over by the macronucleus which, like the body cells of the Metazoa, is destined to die.[2] Now since even the elementary details of sexual reproduction, such as the formation and reduction of chromosomes in the gametes, are the same, so doubtless the physiological nature of sex in both the Protozoa and Metazoa is identical.

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[1] Hartmann, M., "Polyenergide Kerne." Biol. Centrbl., 29, 1909.—Goldschmidt, R., "Die Chromidien der Protozoen." Arch. Protistenk., 5, 1904.

[2] This is the quintessence of our oft misunderstood Dualismus theory. See Goldschmidt, R., "Der Chromidialapparat lebhaft funktionierender Gewebezellen." Zool. Jahrb. (An.) 21, 1904.—"Die Chromidien der Protozoen." Arch. Protistenk., 5, 1904.—"Lebensgeschichte der Mastigamöben *Mastigella vitrea* und *Mastigina setosa*." *Ibid.* Suppl. 1, 1907.—"Das Skelett der Muskelzelle von Ascaris usw." Arch. Zellf., 4, 1909.

The Protozoa have provided much material for experimental study in connection with the problems of sex—particularly the Infusoria where classic studies have been made by Bütschli, Hertwig, and Maupas. And since asexual reproduction by simple fission alternates here with sexual processes (conjugation), the material is at hand to solve the problem of the *raison d'être*, and the necessity, of sex in the animal world. The more recent researches of R. Hertwig and his pupils, together with that of Calkins, Woodruff, and Woodruff and Erdmann,[1] has brought us very near to this solution. Woodruff has supplied reliable evidence that it is possible to cultivate *Paramœcium* for year after year through many thousands of generations (theoretically an unlimited number) without conjugation. Bisexual reproduction or fertilization is therefore not an absolute necessity for the continued existence of the species (as is also the case for some Metazoa). It would be wrong, however, to conclude that unlimited reproduction is possible without sexuality. By noting exactly the rate of division of *Paramœcia* which are isolated after each division one can recognize a regular rhythm through all the thousands of generations. At pretty regular intervals[2] the rate of fission falls considerably, and at these periods (termed Periods of Depression by Calkins) the organisms are in danger of death. Fig. 12 illustrates a curve for this rhythm of division with regularly occurring periods of depression. Now Woodruff and Erdmann have made the very important discovery that during each period of depression in *Paramœcium* a reorganization of the nucleus takes place, and compared with the nuclear phenomena during conjugation this is nothing else but a real parthenogenesis.[3] The macronucleus disintegrates and goes altogether, the micronucleus undergoes two typical divisions as at the beginning of conjugation, the only divisions left out being those arising from the bisexuality in conjugation. Finally a new macronucleus is reproduced from the micronucleus exactly as in normal conjugation.

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[1] Hertwig, R., "Über Parthenogenesis der Infusorien usw." Biol. Centrbl., 34, 1914. Earlier papers are cited here.—Calkins, G. N., "Studies on the Life-history of Protozoa." Journ. Exp. Zool., 1, 1909.—Woodruff, L. L., and Erdmann, Rh., "A Normal Periodic Reorganization Process," etc. *Ibid.* 17, 1914; 20, 1916.

[2] According to Jollos the regularity of the periods is not a necessary feature. See "Die Fortpflanzung der Infusorien und die potentielle Unsterblechkeit der Einzelligen." Biol. Centrbl., 36, 1906.

[3] Woodruff and Erdmann apply the new term Endomixis to the process without evident ground for so doing.

These important facts lead to the same conclusions as have already been arrived at by the general survey of sexuality. During the life of the organism there is a massing up of substances in the cell, especially, as the Infusoria show us, in the nucleus. These substances cannot be got rid of, and finally they limit the functions of the cell and lead to its death. Thus a continued existence is only possible for the sex cells whose nuclear material with the essential hereditary substances remains undisturbed as an "emergency ration." In the majority of cases in the Metazoa and Protozoa an essential part of the body is mortal. In the non-cellular Infusoria, however, the protoplasm has evidently the power of getting rid of its harmful stores and consequently the organism as a whole continues its existence whilst the dying trophonucleus is re-established from the sex nucleus.[1] Such is the general outline of the nature and the significance of sexuality. Further

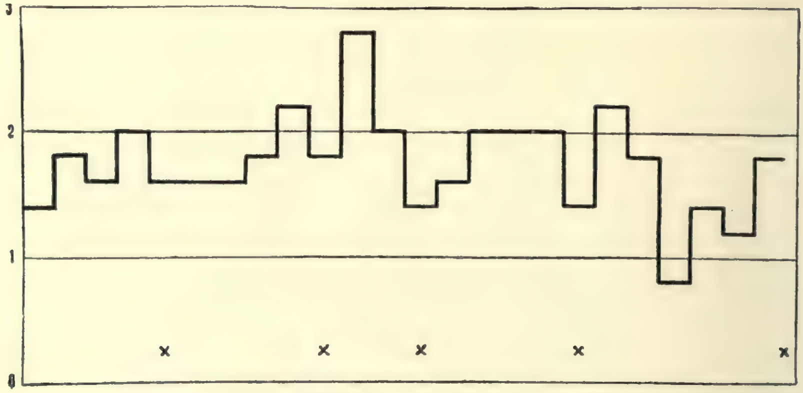

Fig. 12.—Graph showing rate of division of *Paramœcium*. The periods of parthenogenesis are indicated by the crosses. The ordinate gives the number of divisions for every five days, the abscissa gives five-day periods. After Erdmann and Woodruff.

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[1] M. Hartmann certainly demonstrated a long period of non-sexual reproduction without nuclear reorganization for Eudorina. But we are dealing here with a green organism with vegetable type of nutrition, and we do not consider that conclusions can be drawn therefrom which are applicable to animal organisms.—"Unters. uber die Morphologie und Phys. des Formwechsels," etc. Sitzber. preuss Ak. Wiss., 1917.

progress towards a solution of the problem is likely to be essentially chemical in nature. What are the accumulated reaction products, and why do they eventually hinder the continuance of the functions? What is the chemical or physical nature of the system which prevents their extrusion? What is the chemical nature of the living substance of which the above is the physico-chemical consequence, and finally, What is the chemical and physical nature of the substances which are able, unaffected by the wear and tear of function, to continue unconsumed, even replenishing themselves, through the ages?

Although to-day we may not be in a position to supply any firmly established answer to these questions, we can at least say that it is more probable that the definite elucidation of the nature and necessity of sex will be a matter of concepts such as reaction products, catalysis, hydrogen ion concentration, and colloids rather than of rejuvenation, amphimixis, and germinal selection.

We have suggested in the preceding pages that in our first consideration of sexual reproduction we can leave aside the question of bisexual reproduction. This is based on the fact that there are organisms such as certain Phyllopods, Branchiopods, Orthoptera, and Nematoda which are exclusively unisexual, propagating by parthenogenesis whilst their nearest relatives, sometimes even races of the same species, are normally bisexual.[1] It is based further on the fact that Infusoria, Volvocinæ, and also Daphnids can be induced experimentally to reproduce exclusively by unisexual processes, although left to themselves they would reproduce bisexually. Finally, it is based on the well-known facts of artificial parthenogenesis, which show that eggs normally requiring fertilization by spermatozoa can be induced to develop by chemical methods and actually attain perfect development into normal individuals.[2] All this, however, does not alter the fact that bisexual reproduction is the rule in the animal world, as also in the plant world, and that an endless variety of developments and adaptations is present to render fertilization (i.e. the fusion of male and female sex cells) possible. This is sufficient indication that this form of sexuality must be of paramount physiological importance. The only physiological fact known as a result of the work of Loeb, Warburg, and others[1] in connection with artificial parthenogenesis is that one influence of the spermatozoa and also of the artificial methods of chemical parthenogenesis results in the activation of oxidation processes in the egg.

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[1] See later under Parthenogenesis.

[2] Loeb, J., "Artificial Parthenogenesis and Fertilization." Chicago, 1913.

It would appear, therefore, that as a rule developmental processes cannot be set going unless certain alterations have been produced in the egg by the entering spermatozoan. It is quite unthinkable, however, that the significance of bisexuality is nothing more than this. Were such the case one would be forced to the conclusion that all the complicated processes and adaptations of bisexuality represented only an enormous waste of energy, for it is quite clear that in natural parthenogenesis the external stimulus to development is not required.

The consequence of this position is that attempts have been made to link up the phenomenon of bisexuality with the nature of heredity and variation—an effort the best expression of which is found in Weismann's theory of Amphimixis. We consider that this, together with related theories, is essentially formal in character, and we are inclined therefore to suspend judgment until suitable experiments have given us more physiological data.

It must not be concealed, however, that the results of Mendelian investigation do point to an increase in variability (and therefore an increase in the material at hand for selection) as a result of bisexual reproduction increasing the number of factor combinations. And perhaps the teleological significance of bisexuality is thus visible here.

Another source from which important insight may come lies in the remarkable facts of sexuality in the lower fungi as discovered by Blakeslee and Kniep, and happily there is also the possibility here of taking up the problem experimentally.[2]

In the following chapters we shall deal with that predominant feature of living organisms, the separation of the sexes. It comprises that vast array of biological facts and problems which are generally known and discussed under the title of sex problems.

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[1] Loeb, J., l.c.—Warburg, O., "Beobachtungen über Oxydationsprozesse im Seeigelei." Ztschr. physiol. Chemie, 57, 1908.

[2] Blakeslee, W. F., "Sexual Reproduction in the Mucorineae." Proc. Am. Ac., 40, 1904, and many further publications.—Kniep, H., Über morpholog. und physiolog. Geschlechts-differenzierung." Verh. phys. med. Ges. Würzburg, 1919, and further publications. Comprehensive summary of the whole problem: Hartmann, M., "Ergebnisse und Probleme der Befruchtungslehre in Lichte der Protisten forschung." Die Naturwissenschaften, 1918.—Hertwig, G., "Das Sexualitätsproblem." Biol. Centralbl., 41, 1922.

SECTION II.—THE BASIC FACTS

When we refer to the problems which arise out of the fact of bisexuality, we mean only those sexual problems in the narrower sense which can be included in the question of the Heredity and Determination of Sex. Since bisexual reproduction exercises perhaps the most fundamental influence on the structure, physiology, and behaviour of animal life, it is not surprising that the biology of animal reproduction is one of the richest domains in the science, and it is far from our intention even to refer to all the chief data.

We assume therefore a knowledge of its main characteristics, and detail only such facts as are necessary for our own particular problem.[1] We have called this more restricted problem the Heredity and Determination of Sex. The elementary fact of the problem is that, with certain special exceptions, an apparently similar process of fertilization with apparently identical eggs results in the production of two kinds of individuals (male and female) in approximately equal proportions. Very often these two sorts of individuals differ so much from each other that, without special knowledge of their relationship, one has repeatedly mistaken them for different species or even different genera. The regularity and apparent fixity of this process suggests that it rests upon some elementary mechanism of heredity. And so the first problem of bisexuality takes the form of an enquiry into the mechanism which determines the regular separation of the sexes. This fundamental problem of sex heredity is to-day solved, as the following pages will tend to show.

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[1] A very extensive exposition of this subject is given by Meisenheimer, J., "Geschlecht and Geschlechter im Tierreich," 1 Bd. Jena, Fischer, 1922. See also Cunningham, J. F., "Sexual Dimorphism in the Animal Kingdom." London, 1900.—R. G. Goldschmidt, "Die Fortpflanzung der Tiere." Leipzig, Teubner, 1909.

CHAPTER II

THE MECHANISM OF NORMAL SEX HEREDITY

EVERY one knows to-day how Gregor Mendel discovered in the sixties of the nineteenth century the mechanism by which certain hereditable characters were handed on from one generation to another in a regular and orderly manner. Now the heredity of sex is a phenomenon in which—just as in the Mendelian experiments—certain classes of individuals (the two sexes) appear in definite numerical relations (usually equal numbers). It was quite natural then that an attempt should be made to apply the laws of Mendelian inheritance to the problem of the inheritance of sex. Mendel himself was responsible for the suggestion and that at a time when nothing was known of the complicated cytological phenomena of fertilization, maturation, and of the chromosomes. His remarks concerning this problem run as follows :—[1]

"Is it pure accident that the plants in question occur in the proportions 52 : 203 or 1 : 4, or, has this ratio the same significance as in the first generation of the hybrid with variable descendants? I am inclined to doubt the latter in view of the peculiar inferences which would result. On the other hand, the question cannot be so easily dismissed when one bears in mind that the Anlage for the efficient development either of the pistil or the anthers must already be expressed in the organization of the original cells from which the plants were developed, and moreover that this difference in the original cells might possibly be due to the fact that both ovules and pollen cells differed in regard to their sexual Anlage."

Soon after the rediscovery of the laws of Mendel in 1900, the idea was again forthcoming, first from Strasburger and Castle and then more especially as the result of the work of Geoffrey Smith, Bateson, and Correns. Since for the proper comprehension of this subject a knowledge of the laws of Mendel is essential, the oft-stated principles are recapitulated here for the sake of readers who are not biologists.

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[1] Mendel, G., "Letter to C. Nägeli (1870)." Abhdlg. d. K. Sächs. Ges. Wissenschaft. Math.-Phys. Kl. 39 III, 1905, S. 241 (edited by C. Correns).

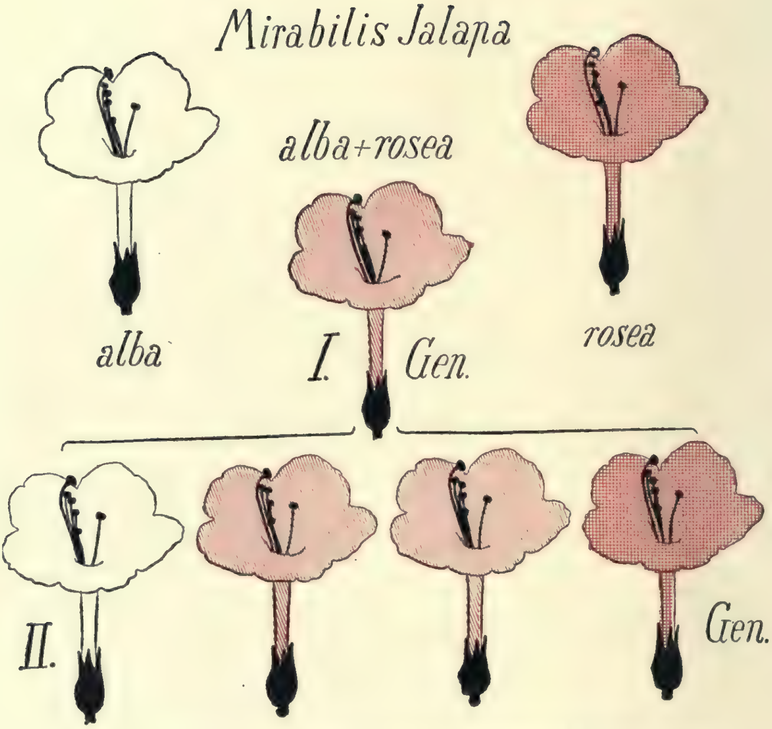
Mirabilis Jalapa
alba+rosea
alba
I. Gen.
rosea
II. Gen.

FIG. 13.—Mendelian segregation in the flower-colour of *Mirabilis jalapa*.
After Correns.

[*To face page* 25.

a. The Laws of Mendelian Inheritance

Mendel's starting point was the conviction that the only way to discover a law of heredity was to cross a race containing a certain pure breeding character with another containing a corresponding, albeit different, character and to follow the condition of this pair of characters in the hybrid and its progeny. For this purpose he used different races of the edible pea. We shall take another case for preference, one that was studied later by Correns.

There are two races of the Marvel of Peru (*Mirabilis jalapa*, a garden plant) which differ in one rather obvious character. One possesses red flowers, the other white. If these two types are crossed, the resulting hybrid (the so-called first filial or F_1 generation) is a bright pink. The two initial characters appear to have become mixed. If two of these hybrids are now crossed, the resultant seeds give rise to three kinds of plants—some with white, some with red, and some with bright pink flowers, and these different kinds of plants occur in the proportions $\frac{1}{4}$ white, $\frac{2}{4}$ bright pink, and $\frac{1}{4}$ red (Fig. 13). If these F_2 (second filial) generation plants are bred further by self-pollinating the flowers so that no crossing occurs, it becomes evident that the F_2 white-flowering plants are pure—they only produce white-flowering plants. The same thing applies to the red-flowering plants, which are therefore pure for redness. The pink-flowering plants are, however, exactly like their F_1 hybrid parents; they give red-, white-, and pink-flowering plants in the same proportions as before. Through segregation, therefore, in the second hybrid generation the original parental types are obtained again in the pure condition. Mendel discovered the simple key to these facts; a basis on which a whole science has been built up since his work became known.[1] If two similar parents reproduce offspring identical in character, it is due to the fact that their sex cells or gametes bring together at fertilization the same kind of heritage (the same complex of hereditable factors). For example, the male and female gametes of the red-flowering plant bear the factor A for redness. The progeny is therefore again AA in character. The same thing holds good for the white-flowering plant, all of whose gametes will contain the white factor a. In the hybrid cross, however, the gametes of the red parent carry the factor A and the gametes of the white parent the factor a; the consequence of fertilization is that the resultant seeds possess the characters, A and a, and the plants which grow from them are Aa in constitution. Since some of the progeny of these hybrids are again pure red or white in character, it must mean that some of the gametes of such hybrids contained the A factor and some the a factor, so that there was a possibility of fertilization giving AA and aa again. In other words this means that in the hybrid the hereditable factors do not mix but remain pure and independent, and they are handed over to the gametes of the hybrid in the same state as they entered. This is the substance of the first law of Mendel—the doctrine of the "purity of the gametes"—or the law of segregation.

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[1] Mendel, G., "Versuche über Pflanzenhybriden." Reprint in Ostwald's Classics. Text-book Exposition: Bateson, W., "Mendel's Principles of Heredity." Cambridge, 1909 (3rd Imp., 1913).—Baur, E., "Einführung in die experimentelle Vererbungsgesetze." Berlin, 1912.—Darbishire, A. R., "Breeding and the Mendelian Discovery." London, 1911.—Goldschmidt, R., "Einführung in die Vererbungswissenschaft." 3 Aufl. Leipzig, 1920.—Haecker, O., "Allgemeine Vererbungslehre." 2. Aufl. Braunschweig, 1912.—Plate, L., "Vererbungslehre." Leipzig, 1913.—Punnett, R. C., "Mendelism." London, 1911.

In our example we saw that the red flower plant AA crossed with the white flower variety aa gave the pink flower hybrid Aa. In the formation of the gametes by the hybrid these factors A and a are again separated. If the mechanism of this separation were subject to the laws of chance, half the gametes should bear the factor A and half the factor a, and this would hold good for the female gametes, the ovules, as well as for the pollen cells. An ovule of the constitution A could be fertilized either by a pollen grain with the factor A or one with the factor a, and the same holds good for the ovules of the constitution a. Now if this fertilization is also purely a matter of chance, the number of A ovules fertilized by A pollen grains should be the same as the number fertilized by a pollen grains, and the same thing applies exactly to the a ovules. The result is that one quarter of the fertilization gives AA, another quarter gives Aa, a quarter gives aA, and a quarter gives aa. And this is exactly the experimental result $\frac{1}{4}$ red, $\frac{2}{4}$ pink, and $\frac{1}{4}$ white. Thus the Mendelian segregation finds its explanation in the purity of the gametes, whilst the regular distribution of the classes is the result of combinations according to the laws of chance.

The reason why we did not take Mendel's pea experiments as our first example may now be indicated.

In the case of the Marvel of Peru the F_1 hybrid presents a mixture of the two parent characters in the colour of its flowers, red and white giving pink. In very many cases, however, one of the two parent characters completely dominates the other in the F_1 hybrid, so that this is exactly like one parent in appearance.

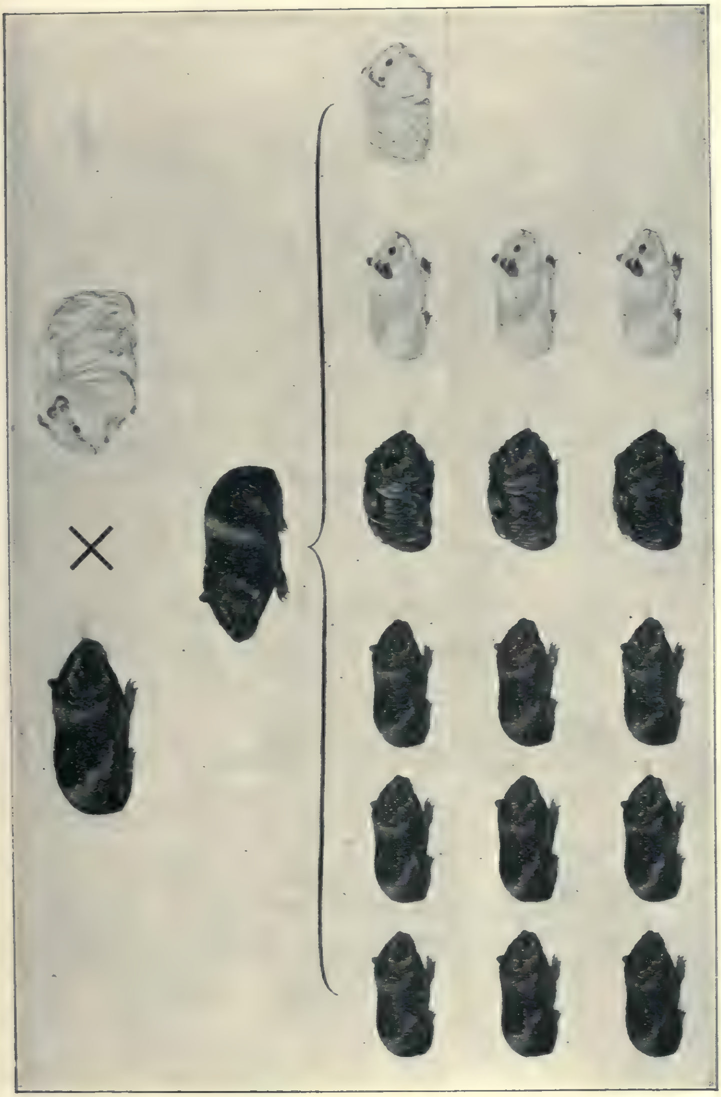

FIG. 14.—Dihybrid Mendelian segregation in the cross black smooth-haired with white long-haired guinea-pigs. Baur-Goldschmidt's wall diagrams.

This character is termed the dominant, the other being called the recessive. In spite of this feature the F_2 generation in these cases segregates in the manner already described above. If we denote the dominant character by D and the recessive by r, then the hybrid has the constitution Dr, and in the F_2 generation we get

¼DD : ¼Dr : ¼rD : ¼rr. Since the DD individuals cannot be distinguished externally from the Dr, the F_2 generation will appear to consist of ¾ individuals with the dominant character and ¼ with the recessive. It is only by the test of breeding that we can find out the real constitution of the individuals with the dominant character. For an example of this type of Mendelian inheritance, we may take the cross between a mallard, with the well-known wild type of plumage, and a white domestic duck. It will be impossible to distinguish the F_1 hybrid generation from the mallard. Evidently wild colour is dominant to white. In the F_2 generation segregation takes place and there will be three wild coloured birds to each white.

The matter is more complicated if pure bred individuals, differing in more than one pair of characters, are crossed. Each pair of characters considered alone shows, however, the typical segregation, and thus, if the gametes are pure for A and a, B and b, and also for C and c, it follows that all the possible combinations of these factors have an equal chance of coming together in the production of the F_2 generation. Suppose we cross an individual AABB with aabb, the F_1 hybrid will have the constitution AaBb. It will produce gametes possessing all the possible combinations of A or a with B or b, and each possibility will occur with equal frequency. Consequently the gametes will be AB, Ab, aB, and ab and equal numbers of each will be produced. This takes place in both sexes, so that in fertilization these four kinds of gametes will have the chance of combining with four similar kinds, resulting in sixteen possible combinations. The scheme can be illustrated as follows :—

AB AB 1	AB Ab 2	AB aB 3	AB ab 4
Ab AB 5	Ab Ab 6	Ab aB 7	Ab ab 8
aB AB 9	aB Ab 10	aB aB 11	aB ab 12
ab AB 13	ab Ab 14	ab aB 15	ab ab 16

If the character indicated by the capital letter is dominant over that represented by the small letter, then out of every sixteen individuals nine should possess both dominant characters (numbers 1, 2, 3, 4, 5, 7, 9, 10, and 13). Three should have one dominant character A and one recessive b (numbers 6, 8, and 14). Three individuals should have the characters a and B (namely 11, 12, and 15), and one should bear both the recessive (number 16).

The segregation in the F_2 generation results therefore in four combinations in the proportions 9 : 3 : 3 : 1. Such a case is illustrated in Fig. 14, where black smooth-haired guinea-pigs are crossed with white Angora-haired guinea-pigs. Blackness is dominant over whiteness and smooth-hair over Angora-hair. The F_2 generation consists of nine black smooth-haired, three black Angora-haired, three white smooth-haired individuals and one white Angora-haired individual.

In the above way one can easily reckon the expected result for any number of pairs of characters. If, for example, the two individuals crossed differed in three pairs of characters, the constitution being AA, BB, CC, and aa, bb, cc respectively, the hybrid would have the constitution AaBbCc and produce eight different kinds of gametes ABC, ABc, AbC, aBC, Abc, aBc, abC, and abc. Fertilization would give sixty-four possible combinations, and if A, B, and C were dominant to a, b, and c respectively, the F_2 result would be :—

27	individuals with all three dominant characters	(ABC)
9	,, ,, two dominant and one recessive character	(ABc)
9	,, ,, ,, ,, ,, ,, ,, ,,	(AbC)
9	,, ,, ,, ,, ,, ,, ,, ,,	(aBC)
3	,, ,, one ,, ,, two ,, characters	(Abc)
3	,, ,, ,, ,, ,, ,, ,, ,,	(aBc)
3	,, ,, ,, ,, ,, ,, ,, ,,	(abC)
1	,, ,, three recessive characters	(abc)

A second Mendelian law follows from these last examples, namely, that in the offspring of hybrids all the characters in which the parents of the hybrids differed may recombine freely in all the possible combinations. The principle of the independent behaviour of unit characters, as they are called, is of the greatest importance in the study of heredity, but further details are not necessary for the understanding of the sex problems.

b. Sex as a Mendelian Character

We have seen the result of crossing two similar hybrids; let us now enquire into a very important cross from our point of view, namely, that between a hybrid and one of its parents, a so-called back-cross. If the same example is used and the pink-flowering hybrid of *Mirabilis jalapa* is fertilized with pollen from the white-flowering parental race, we shall have carried out a Mendelian back-cross. We know that the hybrid should produce gametes pure for A and for a. If these are fertilized by gametes all of which are pure a in type, there should be just as many fertilized by A gametes as a gametes, and the result should be Aa and aa seeds in equal numbers. These would give pink-flowering plants and white-flowering plants in equal numbers; in other words, the same types as the parents used in the cross. What would be the result of a back-cross if the hybrid were not intermediate in character but like the dominant, as in the example of the ducks? The hybrid might be termed Aa in constitution, A being dominant over a, and the hybrid would resemble externally the parent which supplied the character A. If this hybrid were crossed with the dominant parent—Aa × AA, we should in the resulting offspring obtain equal numbers of AA and Aa individuals, the mechanism being the same as in the former experiment. But since the hybrid Aa is outwardly at least like the pure dominant AA, all the offspring would look alike although two types were really present. The corresponding back-cross between the hybrid and the recessive parent = Aa × aa—would give progeny of the distinct types Aa and aa in equal numbers.

This shows us that if we back-cross a hybrid with its recessive parent, we obtain offspring of the same kind as those used in the cross and in equal numbers.

It will be noticed at once that this result is very similar to the phenomenon of normal sex inheritance. In both cases the parents present a typical difference, and in both cases the offspring are of two types, presenting the same difference, and occurring in equal numbers. If then maleness and femaleness be inherited like Mendelian factors, sex inheritance could be regarded as a back-cross in which one sex is hybrid for the sex factors, that is, containing both dominant and re-

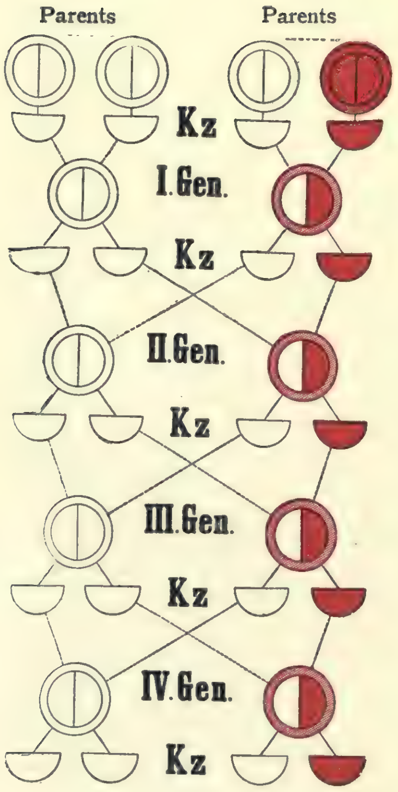
Parents
Parents
Kz
I. Gen.
Kz
II. Gen.
Kz
III. Gen.
Kz
IV. Gen.
Kz

FIG. 15A.—Diagram of the back-cross of a Mendelian hybrid (between a red and a white-flowering type) with its recessive (white-flowering) parent, four generations.

Each plant is represented by a disc, the border of which shows the flower colour. The semicircles enclosed represent the germ cells from which the plant has arisen. In the same way the semicircles kz represent the germ cells resulting from the plants represented by the discs above them.

After Correns.

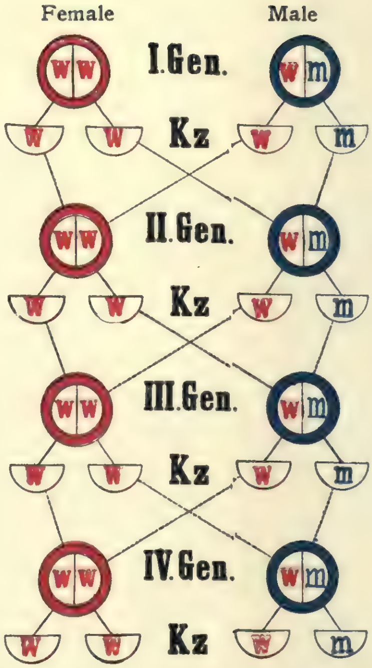
Female
Male
I. Gen.
w w
w m
Kz
w
w
w
m
II. Gen.
Kz
III. Gen.
Kz
IV. Gen.
Kz

FIG. 15B.—Sex determination according to the scheme of a back-cross of a Mendelian hybrid, four generations.

Each plant is again represented by a disc. The colour of the border indicates the sex which manifests itself (blue = male, red = female). The semicircles enclosed represent the germ cells from which the plants have arisen, and their tendencies (m = male, w = female) In the same way the semicircles kz represent the germ cells resulting from the plants represented by the discs above them.

After Correns.

[*To face page* 31.

cessive factors, whilst the other sex is pure, containing only the recessive factor.

If we denote the factor for maleness by M and consider it as dominant to femaleness m, the two sexes could have the constitution Mm = ♂ and mm = ♀. The diagram in Fig. 15 explains the assumption of an identity between the back-crossing of *Mirabilis* and sex inheritance.

In describing Mendelian inheritance certain other terms are used which it will be necessary to explain here. The hybrid is referred to as the heterozygote (i.e. the zygote resulting from the union of gametes bearing different Mendelian characters), whilst the pure form is the homozygote (i.e. the result of the union of gametes bearing the same Mendelian character). In the example given above the male sex was considered to be the heterozygote and the female the homozygote. But it will be obvious that theoretically there is just as much reason for the female being the heterozygote (Ff, if F = femaleness and f = maleness) and the male the homozygote (♂ ff). We shall see that in nature both types are actually present, the first cases of sex inheritance to be analysed belonged to the type with male heterozygotism, whilst almost at the same time the type with female heterozygotism was discovered. The first analysis which brought experimental evidence for regarding the inheritance of sex as a Mendelian back-cross was Correns' investigation[1] with two species of Bryony. Since, however, this case concerns plants and is moreover complicated in various ways, its discussion will not be pursued here. The experiments which, in company with cytological discoveries, led to the elucidation of the problem were the investigations into cases of so-called sex-linked inheritance. The classical example is Doncaster's work on the currant moth, *Abraxas grossulariata*.[2]

A rare light-coloured variety of this moth occurs—the variety *lacticolor*—which is a kind of albino and usually turns up only in the female sex (Fig. 16). When *lacticolor* ♀ were crossed with *grossulariata* ♂, the individuals of the F_1 generation were of the *grossulariata* type and both sexes were present. The *grossulariata* character is evidently dominant to *lacticolor*.

---

[1] Correns C., "Die Bestimmung und Vererbung des Geschlechts." Berlin, 1907.

[2] Doncaster, L., and Rayner, Ch. H., "On Breeding Experiments with Lepidoptera." Proc. Zool. Soc. London, 1906.

In the F_2 generation both types were found and in the proportions 3 : 1, there being eighteen *grossulariata* to seven *lacticolor*. Whilst, however, the *grossulariata* forms were of both sexes as was to be expected, the white *lacticolor* forms were all female. When the F_1 (heterozygotic) *grossulariata* males were back-crossed with *lacticolor* females, the result was the expected one, the offspring being half *grossulariata* and half *lacticolor*, but both types were of both sexes, the numbers actually being 63 *grossulariata* ♂, 62 *grossulariata* ♀, 65 *lacticolor* ♂, and 70 *lacticolor* ♀. In this cross the *lacticolor* males first appeared. Now when one of these *lacticolor* males was paired with an F_1 hybrid *grossulariata* female the offspring were naturally half *grossulariata* and half *lacticolor* in type, the actual numbers being 145 and 130, but the *grossulariata* forms were all male and the *lacticolor* forms all female. On the other hand, when these *lacticolor* males were crossed with the wild *grossulariata* females, which might be expected to be pure (owing to the rareness of the *lacticolor* variety in nature), the same result was obtained, all the *grossulariata*, 19, were male, and all the *lacticolor*, namely 52, were female.

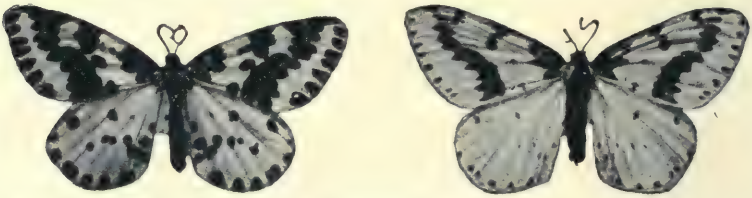

FIG. 16.—*Abraxas grossulariata* (left side) and the variety *lacticolor* (right). After Doncaster.

It would appear, then, that the naturally wild *grossulariata* females were after all heterozygotic for the character *lacticolor*, and that the *grossulariata* character G was dominant to the *lacticolor* character g. But how is the relationship of sex to the colour pattern to be explained? Bateson and Punnett showed that it would be clear if one assumed that maleness and femaleness were Mendelian characters and that the female was always heterozygotic for sex (femaleness acting as dominant), the male being the homozygote. If F signifies femaleness and f absence of femaleness, that is maleness, then all females will have the constitution Ff and all males will be ff. If the further assumption is made that both the dominant characters repel one another, so that they are never found in the same gamete, all the above crosses are explained.

The last cross, that between wild *grossulariata* ♀ and *lacticolor* ♂, as also the similar one in which F_1 *grossulariata* ♀ are used, can be analysed as follows:—

The *grossulariata* females have the constitution GgFf, the *lacticolor* males are ggff. The former, as a result of repulsion, give gametes of only two kinds Gf and gF, whilst the gametes of *lacticolor* are all of one sort—gf. The result will be that the offspring are half Gfgf and half gFgf, that is *grossulariata* males and *lacticolor* females.

If we cross the hybrid *grossulariata* F_1 generation first referred to amongst themselves, the constitutional formulæ will be as follows:—

F_1 *grossulariata* ♀ GgFf, F_1 *grossulariata* ♂ Ggff. The gametes in consequence of repulsion will be—

Gf and gF   Gf and gf

and fertilization will give equal numbers of the combinations—

GfGf = *grossulariata* ♂
Gfgf = ,, ♂
gFGf = ,, ♀
gFgf = *lacticolor* ♀

Again, let a *lacticolor* ♀ ggFf be crossed with a hybrid *grossulariata* ♂ Ggff. The gametes would be—

gF and gf   Gf and gf

The following four combinations would result in equal numbers:—

gFGf = *grossulariata* ♀
gFgf = *lacticolor* ♀
gfGf = *grossulariata* ♂
gfgf = *lacticolor* ♂

These experiments support the assumption that the inheritance of sex corresponds to a Mendelian back-cross (in this case with heterozygotism of the female) for *a second pair of factors has been followed whose fate is linked in the closest manner with that of the sex factors.* During recent years numerous cases of sex-linked inheritance have been made known and *all lead to the same conclusion; the normal distribution of the sexes is determined by a "mechanism of heredity" similar to that of a Mendelian back-cross.*

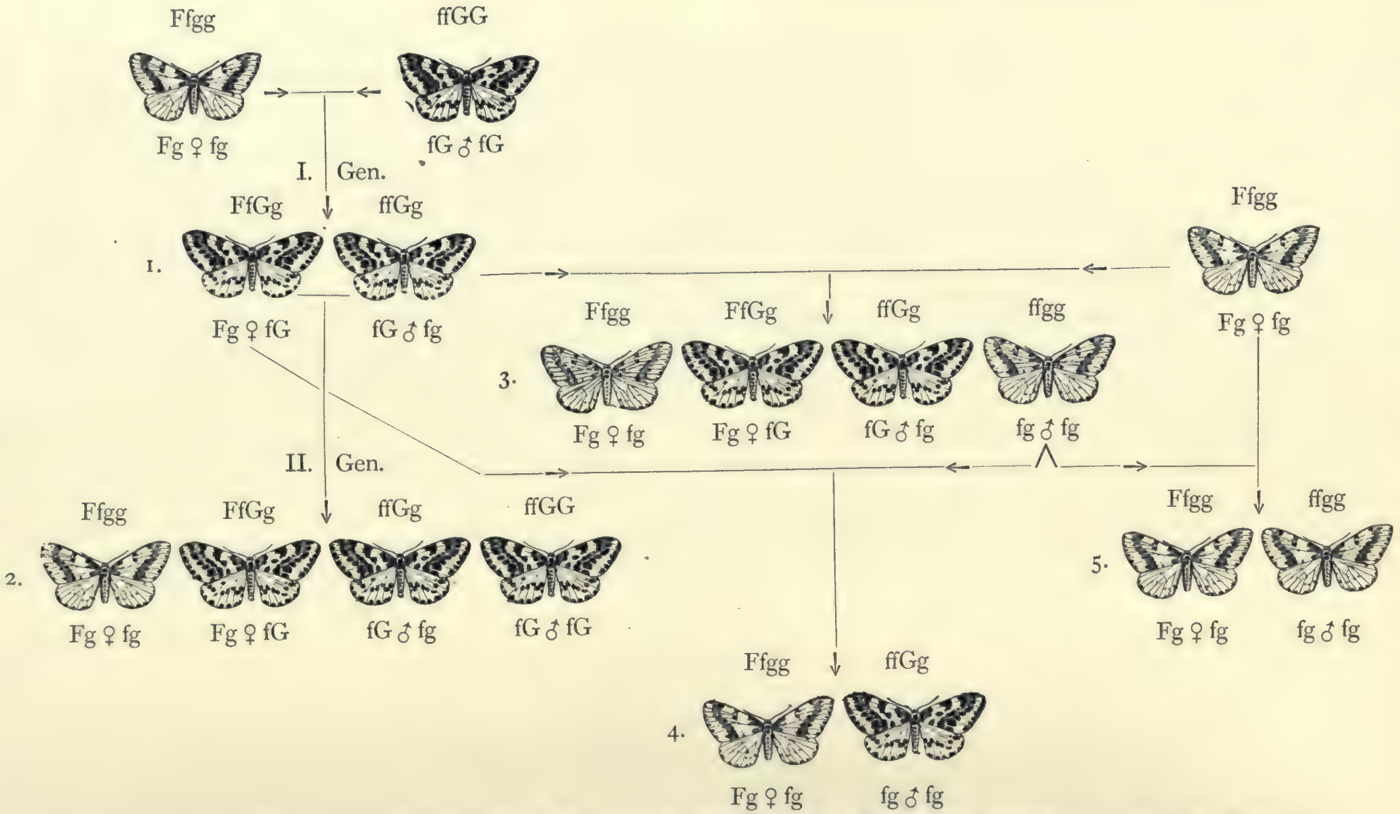
Ffgg
ffGG
Fg ♀ fg
fG ♂ fG
I. Gen.
FfGg
ffGg
I.
Fg ♀ fG
fG ♂ fg
Ffgg
Fg ♀ fg
3.
Ffgg
FfGg
ffGg
ffgg
Fg ♀ fg
Fg ♀ fG
fG ♂ fg
fg ♂ fg
II. Gen.
2.
Ffgg
FfGg
ffGg
ffGG
Fg ♀ fg
Fg ♀ fG
fG ♂ fg
fG ♂ fG
5.
Ffgg
ffgg
Fg ♀ fg
fg ♂ fg
4.
Ffgg
ffGg
Fg ♀ fg
fg ♂ fg

Fig. 17.—Diagram illustrating Doncaster's crosses with *Abraxas grossulariata* (dark) and its variety *lacticolor* (light colour in diagram).

The heredity formula of each moth is placed above it, whilst below and to right and left of the signs indicating sex are the formulæ of the germ cells. Lines connect the parents with each other and with the progeny.

One sex is hybrid or heterozygotic for a sex factor and therefore produces two kinds of germ cells, the other is homo-zygotic and only produces one kind of germ cell. What these sex factors really are and how they determine the sex does not concern us here, since we are dealing exclusively with the *mechanism* of inheritance and not with that which is actually inherited. Before, however, we examine further cases we must look into another field of investigation which, in conjunction with the breeding experiments, shares in the definite solution of the problem. It is the study of the cytology of the sex cells.

c. The Cytological Side of the Sex Problem

The Mendelian type of inheritance involves the action of processes taking place in the sex cells without demanding where and how in these cells the segregation of the factors is accomplished. It would have been impossible for Mendel to have arrived at any ideas on the subject, because in his time even the foundations of the requisite knowledge had yet to be laid. It was not until after 1875 that the finer details of the history of the sex cells were disclosed. When, however, in 1900 the laws of Mendel were rediscovered, it was not long before decided advances had been made to clear up the relationship between these laws and the structure and processes going on in the sex cells, which had by this time been made known.

And so it came about that the mechanism of the distribution of the sexes was also unveiled by these cell studies. To comprehend the matter, a knowledge of the life history of the sex cells is necessary or, more correctly, a knowledge of their most interesting constituents, the chromosomes. A short recapitulation of the most important facts in this field is appended for non-biologists.

1. *The Chromosomes in Maturation and Fertilization and as Carriers of the Mendelian Factors*

The investigator who studies cell life is always struck by the remarkable ability of the cells to reproduce by fission — the division being of a highly characteristic kind. The essential feature is the exact halving of the two chief constituents of the cell, the protoplasm and the nucleus, so that two daughter cells result which, except for size, are exactly like the mother cell. In the majority of cases, in both the plant and animal kingdoms, cell division is not a simple halving but is accomplished by a complex process called karyokinesis. This is initiated by the division of a small body, the centrosome, which is situated outside the nucleus. Round the dividing centrosome a star or astral figure develops in the protoplasm and soon becomes double as the two centrosomes formed by division gradually separate. In the meantime complicated changes have taken place in the nucleus, with the result that the most important constituent (termed chromatin because of its affinity for certain dyestuffs) appears in the form of a definite number of curved or straight rods—the chromosomes. In Fig. 18 we have taken the number of these bodies as four.

The nuclear wall now disappears and the chromosomes arrange themselves in a row at the equator of the bipolar astral figure, the so-called amphiaster. Each chromosome then splits along its length and the halves gradually separate, migrating to the opposite poles until they are in the proximity of the centrosomes. From now on the events are the reverse of those which gave rise to the chromosomes, the latter gradually lose their identity, a new nucleus is formed at each end of the spindle, the radiations disappear, and the division of the protoplasm results in two cells similar to the original one.

The most striking feature of this process is the appearance and division of chromosomes, and upon these bodies the interest of cytology has been focussed to an ever-increasing degree since their discovery. Their conduct during fertilization leads to the conviction that they are the carriers of substances which are bound up in the closest manner with heredity, and to anticipate we can say with certainty to-day that they are the bearers of the Mendelian factors. The following is an outline of the chief facts pointing to this conclusion :—

When fertilization takes place a male sperm cell penetrates into the female egg cell. Both cells, the so-called gametes, in spite of their very different form, consist of the typical cell constituents—nucleus and cytoplasm. Many sperm cells, however, have the form of a long fibre with a swollen head which consists (as is shown by the origin of the sperm cells) of the nucleus. The rest of the sperm—the middle piece and tail—corresponds to the cytoplasm. Now in many cases it has been observed that at fertilization only the head of the sperm cell penetrates the egg (and correspondingly in the higher plants only the nucleus of the pollen tube), the tail being thrown off. Inside the egg protoplasm the head of the sperm cell takes up the form of an ordinary nucleus and fuses with the nucleus of the egg cell. Since, however, the characters of both parents are brought together and handed on to the offspring at fertilization, it follows

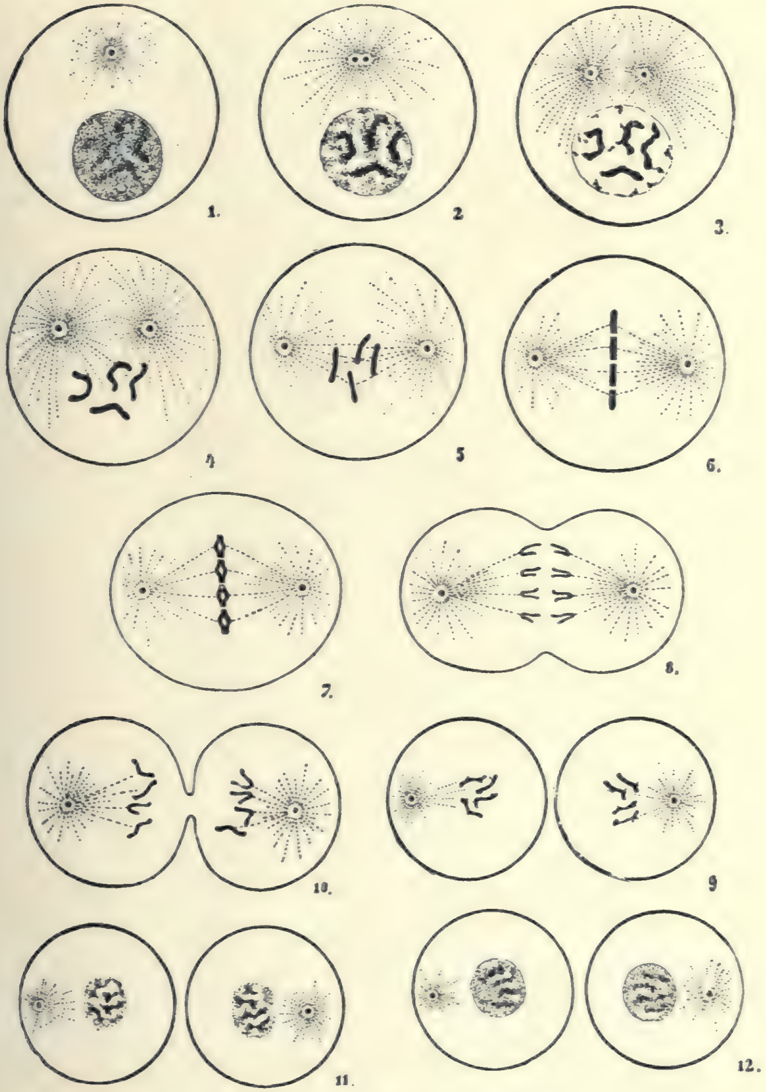

Fig. 18.—Diagram of mitotic cell division.

1-3, formation of the chromosomes in the nucleus; 4, nuclear wall disappears; 5 and 6, formation of the equatorial plate; 7, 8, and 10, divergence of the chromosome halves; 9, 11, 12, reconstruction of the daughter nuclei.

From Goldschmidt.

from the above that these characters must have been contained in some way in the nuclei of the gametes.

It is reasonable, therefore, to look for the carriers of heredity in the nucleus, and a further inspection of the processes of fertilization shows where they lie. We made the statement above that the nuclei of the two gametes fuse. Often, however, this is not literally the case and the two nuclei lie side by side (Fig. 19).

The further development of the organism, which is initiated by the act of fertilization, consists in a long series of cell divisions starting soon after this act. It is possible for the cell division figure (the karyokinetic figure) to form without the nuclei having fused; the chromosomes, however, appear as usual. But they appear in each nucleus separately, and in the example illustrated (Fig. 19) there are two chromosomes in each. The completed karyokinetic figure contains, therefore, a number of chromosomes (here four) of which half have come from the egg cell and half from the sperm cell. In the following stage all these are split lengthwise and distributed in the usual way to the two daughter cells. Thus half the chromosomes received by each are maternal and half paternal, and so it goes on during all the further cell divisions. Now as a result of fertilization the characters of both parents are inherited by the offspring, but we have just seen that the chromosomes are the only structures which are received by all the cells of the offspring in an equal manner from the two parents. We must conclude therefore that the inherited characters are localized in the chromosomes.

So far we have not laid any stress upon the number of the chromosomes, but this is not an indifferent matter. It has been shown that for all species of animals and plants there is a typical and constant number. A parasitic Nematode from the horse exhibits four in all its dividing cells, man probably twenty-four, a tomato also twenty-four, a *Solanum nigrum* (deadly nightshade) seventy-two, and so on. In other words, each species of living organism possesses a characteristic number of chromosomes in the nucleus of its cells. We have seen above that when fertilization takes place two nuclei fuse. If these had also possessed the typical number of chromosomes, the result would be that the fertilized egg contained double the normal number and this would apply to all the cells resulting from it, including the sex cells. The consequence would be that in the next generation the

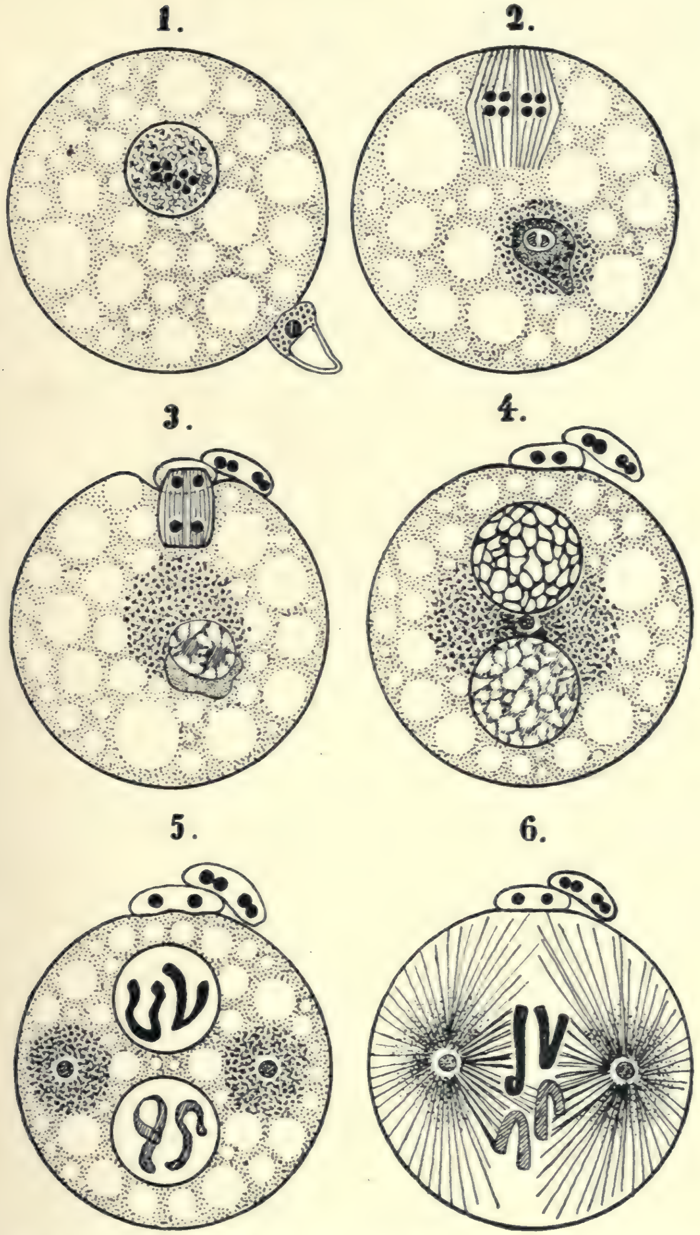

Fig. 19.—Fertilization of the *Ascaris* egg. (The maternal nucleus and chromosomes in black, the paternal shaded.)

1, penetration of the spermatozoan; 2, the first maturation division of the egg nucleus; 3, the second maturation division; 4, male and female pronuclei; 5, appearance of the two chromosomes in each nucleus; 6, distribution of the chromosomes in the first division figure.

From Goldschmidt.

chromosome number would be four times that of the grandparents, and so on. But if this is not the case, and the chromosome number, as we have stated above, is constant for any particular species, this constancy can only be attained in one way, viz. by some arrangement which halves the chromosome number of the sex cells before their union. Such an arrangement actually exists, and consists in a special reduction division which each sex cell must undergo before it is capable of fertiliza-

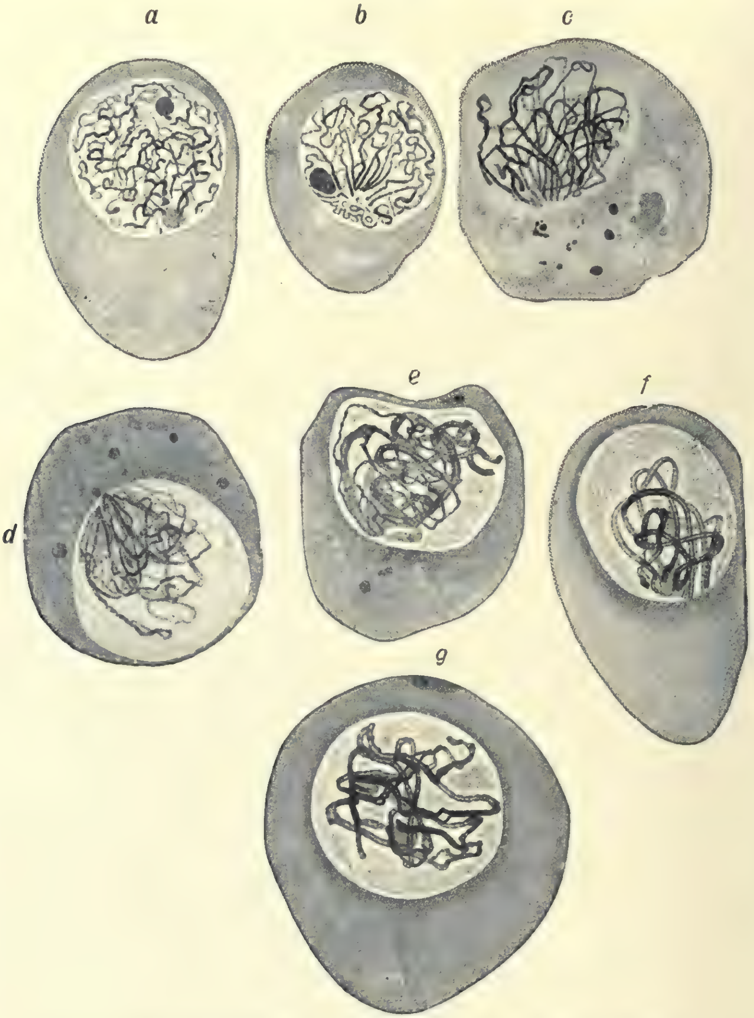

FIG. 20.—The synaptic phenomena in the oogenesis of *Dendrocœlum*.

a, b, formation of the chromosomes; c, disposition for parallel conjugation; d, e, the conjugation; f and g, the bivalent chromosomes become visible.

After Gelei.

tion, i.e. is mature. As a result of this reduction division half the chromosomes are removed from the cell.

It would be very natural to ask if and how this removal of half the chromosomes influenced the mass of hereditary material in the nucleus. The answer to this is bound up with the events which take place during the maturation of the sex cells. Every egg or sperm cell undergoes two special divisions, the maturation divisions, before it is ripe. Now at the very commencement of these divisions, when the chromosomes become visible in the karyokinetic figure, only half the normal number are to be seen; but at the same time these elements are distinctly different from the ordinary chromosomes. On account of a frequently occurring four-partite structure they have been termed tetrads. Their origin must be made quite clear before their distribution in the maturation divisions can be properly understood.

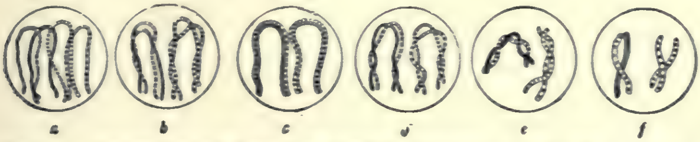

FIG. 21.—Diagrammatic sketch of parallel conjugation of the chromosomes. After Grégoire from Goldschmidt.

To this end let us follow the condition of the chromosomes in the sex cells back to the point where these cells were produced by the last divisions of the oogonia or spermatogonia—the mother cells of the definitive sex cells. The point referred to is that where the period of growth begins. The chromatin from this stage on undergoes curious changes, which begin with a compact entanglement of the chromatin fibre, and end with the appearance for the first time of the reduced number of chromosomes in the form of tetrads. The stage has been termed Synapsis, and some of the phenomena which take place are illustrated in Fig. 20. There can be no doubt that the halving of the chromosome number to the number of the tetrads takes place here. There are, however, very varied opinions as to the exact nature of these processes, and it will be sufficient here to state one of the simplest theories—the formation of tetrads as diagrammatically represented in Fig. 21.[1]

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[1] A general and critical review of the zoological and botanical literature on the maturation divisions and the synaptic phenomena has been given by Grégoire, V.,

Four chromosomes are taken as the normal number and are distinguished by different markings. These apply themselves side by side in pairs (Fig. 21 b) in such close union that in the so-called bouquet stage double chromosomes are produced, each consisting of two closely bound single ones (Fig. 21 c). The further history consists of a characteristic shortening which in the end leads to the tetrad stage (Fig. 21 d, e, and f) and the condition at the end of maturation. The pseudo-reduction of the number of chromosomes during synapsis consists, therefore, in a union of these bodies in pairs, and each tetrad, whatever be its form before the commencement of the maturation divisions, consists of two united chromosomes. None of the chromosomes have so far been lost. We are now in a position to follow the events of maturation. The essence of the maturation divisions lies in the fact that in one of them the chromosomes which are joined in pairs are separated in such a way that the daughter cells not only have the half number of chromatin elements, but half the actual number of chromosomes present at first. Fig. 22 A-E, and Fig. 23 A-C, give the course of the two maturation divisions in a scheme (the normal chromosome number is taken as six) which applies equally well to vegetable pollen grains as to animal sperm cells. In the egg cell the maturation process is also the same in principle; it is slightly different in fact owing to three of the four resulting cells being very small. They are called the polar bodies and are usually not capable of fertilization.

In the example illustrated the immature sex cell after synapsis contains three chromatin elements, each of which is really formed of two chromosomes (one is figured in black, the other is stippled). It is assumed here that the first maturation division is the one which separates the entire chromosomes; i.e. the reduction division. In B one sees the chromatin elements on the equatorial plate of the karyokinetic figure (only just indicated). In C the migration of chromosomes to the two poles of the cell takes place. The fact that they appear double again is of no special consequence here; it is the preparation for the second maturation division which is often indicated at an early stage.

Each of the daughter cells (Fig. 22 D) now possesses half

"Les cinèses de maturation dans les deux règnes." La Cellule, v., 26, 1910. For more recent literature see Haecker, V., "Allgemeine Vererbungslehre," 2 Aufl., 1912. Also Vejdovsky, F., "Zum Problem der Vererbungsträger." K. Böhm. Ges. Wiss. Prag., 1911-12.

of the chromosomes—three of the six present in the normal cell. Fig. 23 shows the course of the second maturation division which follows along the lines of ordinary cell division, the three chromosomes being split along their length (the split which was indicated at an earlier stage, Fig. 22 C). This so-called equation division, the significance of which is not shown here, has no further interest for us in connection with our present study. The reduction division, in which the entire chromosomes are distributed between two cells, is, on the other hand, of paramount importance.

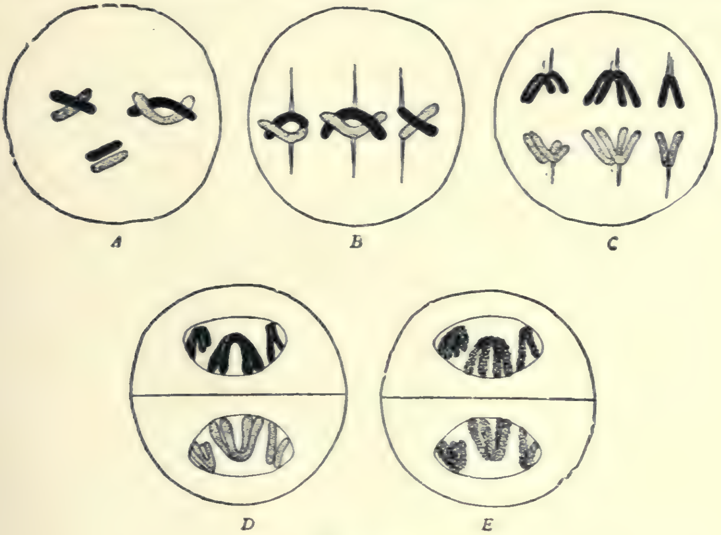

FIG. 22.

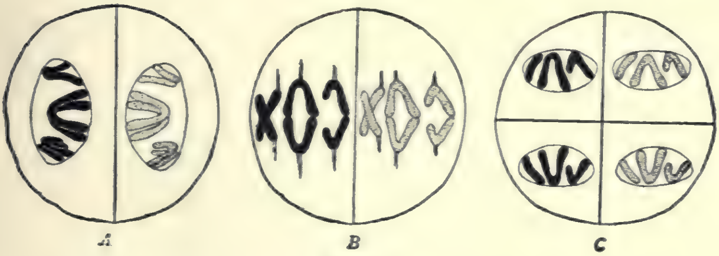

FIG. 23.

FIGS. 22, 23.—Eight successive stages of the two maturation divisions.

The normal chromosome number is six, three of these are shown in black, the other three being stippled. See text.

After Grégoire from Goldschmidt.

In our illustration the division is represented in such a way that one cell receives all the black, the other the stippled chromosomes. This leads to the question as to whether the manner in which the chromosomes are distributed makes any difference. We know that the sperm cell with its half of the chromosomes is capable of handing on the same characters as the egg cell with its half, for in hybridization it is usually of no consequence which of the parent forms is the father or the mother. And we know that each ripe sex cell must carry all the characters in its half of the chromosomes, because the same kind of sea urchin arises from a sea urchin egg by artificial parthenogenesis as from a normally fertilized egg. Furthermore, a fragment of a sea urchin egg containing no nucleus may after fertilization (thus having only the sperm cell nucleus) give rise to a proper sea urchin larva. In both these cases the larva has only the half number (the reduced number) of chromosomes; consequently the chromosomes of the mature egg- (or sperm-) nucleus, must comprise a complete "chromosome equipment." If such is the case, the fertilized egg must have two of each kind of chromosome, one of maternal origin and one that is paternal, and when in due time the sex cells of the next generation are formed each of these will have chromosomes half of which are paternal and half maternal in origin.

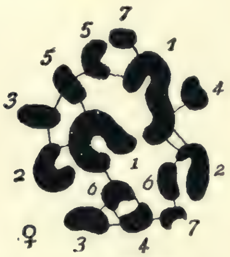

Fig. 24.—Chromosomes of a bug.

Each particular sort is represented by a pair.

After Wilson.

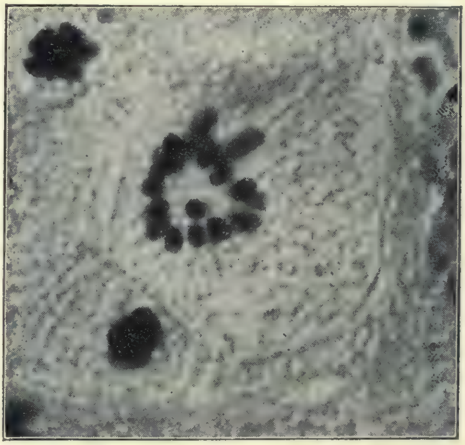

Fig. 25.—Photograph of the chromosomes of a grasshopper.

In the synapsis the chromosomes unite in pairs, whilst in the reduction division the individuals of a pair are separated again and distributed to two cells, so that each cell again possesses all the kinds of chromosomes which were formerly present in duplicate. But half of these are maternal and half paternal in nature, and consequently it is necessary to assume that any two chromosomes pairing in the synapsis stage must be of the same kind, one being maternal, the other paternal.

Fortunately there are cases where the differences between the chromosomes in a nucleus are actually visible to the eye. A case of this kind (in a bug) is illustrated in Fig. 24 and a distinct difference of size is to be noticed. Fig. 25 is a photograph of an actual preparation showing the same feature. Now in examples of this sort it has often been demonstrated that each different size of chromosome is present in duplicate (in the diagram, Fig. 24, these have been indicated with the same numbers). After the pseudo-reduction of the synapsis

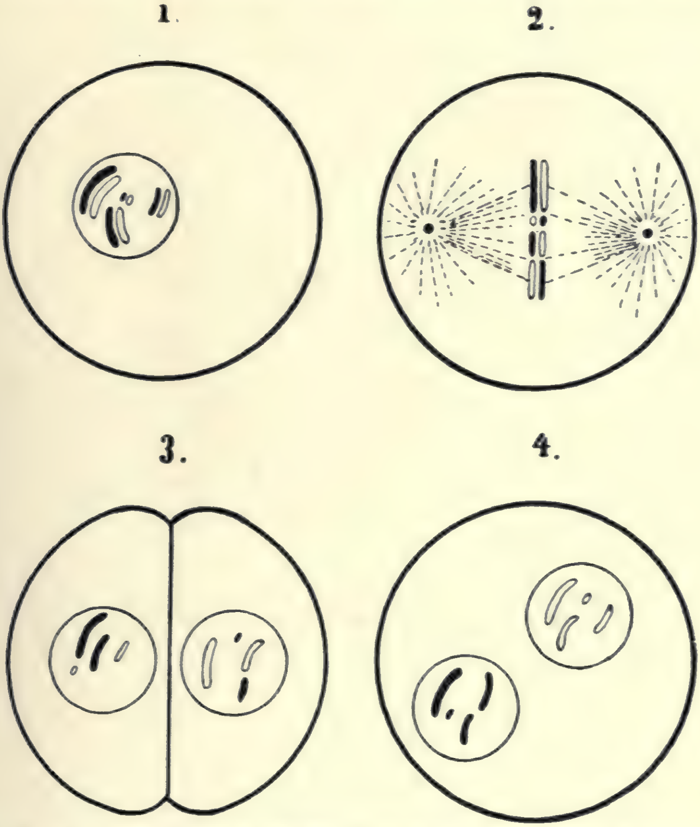

Fig. 26.—Diagram illustrating the relations of the paternal and maternal chromosomes during the maturation divisions.

4, the fertilized egg cell: the maternal chromosomes (white) in the egg nucleus are of four different sizes; in the sperm nucleus there are four corresponding paternal chromosomes (black). 1, the conjugation of the chromosomes during synapsis; 2, the maturation spindle; 3, the mature germ cells.

From Goldschmidt.

stage all the chromosomes, as we have seen, are united in pairs, and these pairs present all the size differences noted at first. Consequently chromosomes of the same size must have united. But, as we saw above, one of each pair of these must be paternal and one maternal in origin—the whole process is diagrammatically illustrated again in Fig. 26, where the paternal and maternal chromosomes are distinguished by their black or white colours respectively.

It will be remembered that the chief facts of the laws of Mendel were explained by distributory processes taking place when the gametes were formed. We have now learned of a mechanism which is responsible for a very definite distribution of the chromosomes in gamete formation. It will not be surprising to learn that the coincidence of both mechanisms can be demonstrated, a discovery first made by Sutton.[1] Assuming that the chromosomes are the carriers of the characters of Mendelian inheritance, and assuming further that one chromosome is responsible for one character, we can deduce in the following manner what takes place in hybridization. Let us take eight chromosomes to be the normal number in the parents of the hybrid; their sex cells will have the reduced number four. Suppose further that of the four chromosomes of the mother, one bears the character for a black fur. We can represent the three chromosomes of the mature egg which bear the other characters of the animal by the stippled chromosomes of the figure and that bearing the black coat character by the black chromosome (Fig. 27, 1). The hybrid father differs from the mother, let us say, by having a white fur, and so the mature germ cells will have the three stippled chromosomes of the figure and one that may be left white (Fig. 27, 2). Fig. 27, 3, represents diagrammatically the fertilization union of these germ cells, and Fig. 27, 4, exhibits the chromosome constitution of the hybrid. The next illustration indicates the course of maturation of the germ cells of this hybrid. In the stage of synapsis the homologous maternal and paternal chromosomes pair, and consequently the chromosome for black fur pairs with that bearing the corresponding character, the chromosome for white fur. The reduction division follows next, and the chromosomes are separated and distributed so that each daughter cell receives three stippled chromosomes and either

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[1] Sutton, W. S., "The Chromosomes in Heredity." Biol. Bull., 8, 1903.

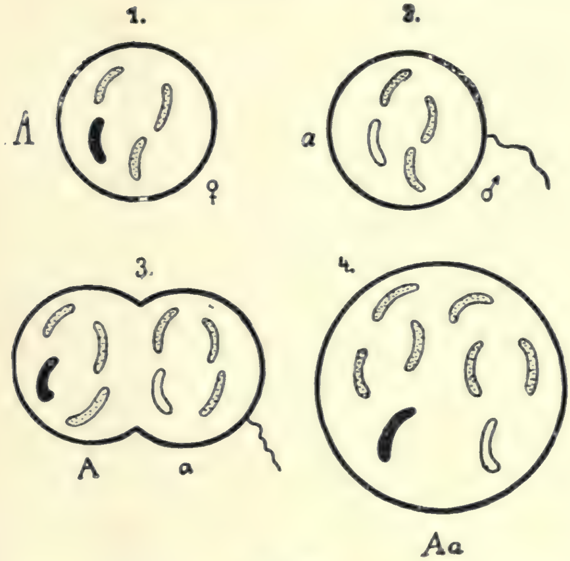

Fig. 27.

1, egg cell of the hybrid parent A; 2, sperm cell of the hybrid parent a; 3, fertilization: 4, chromosomes of the hybrid Aa.

From Goldschmidt.

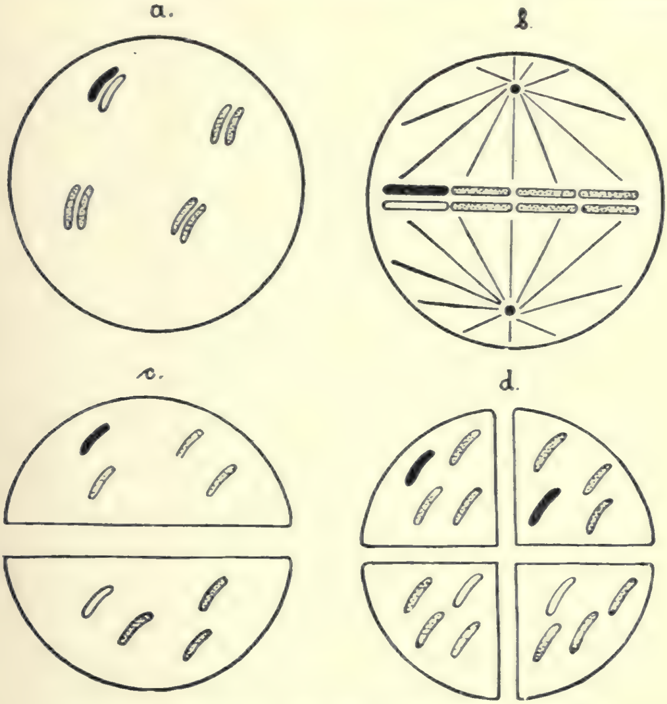

Fig. 28.—Maturation of the germ cells of the hybrid Aa.

a, the synapsis stage; b, the maturation division; c, the two reduced germ cells after the first maturation division; d, the four reduced germ cells after the second division.

From Goldschmidt.

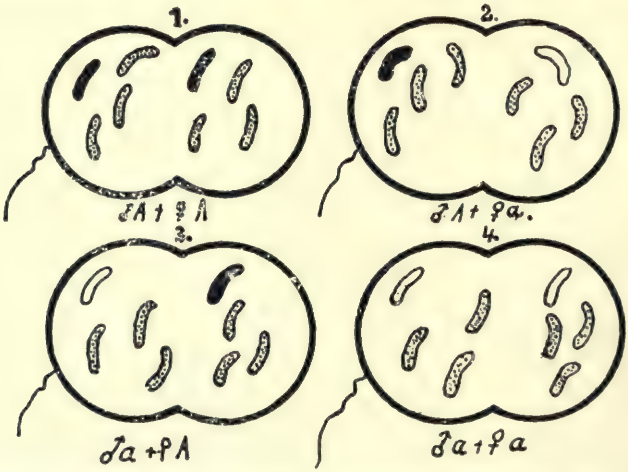
1.
2.
♂A + ♀A
♂A + ♀a.
3.
4.
♂a + ♀A
♂a + ♀a

Fig. 29.—Diagram of the four possibilities of fertilization between the germ cells of the hybrid Aa.

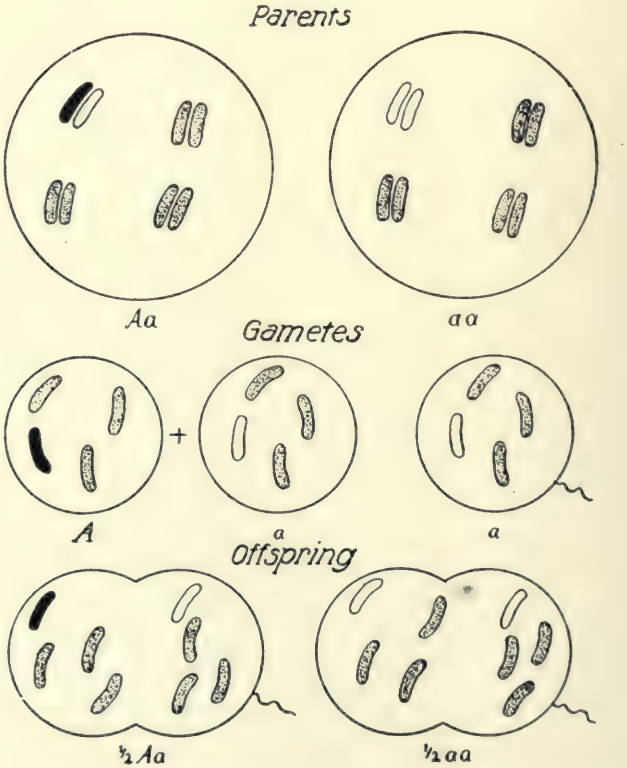
Parents
Aa
aa
Gametes
A
+
a
a
Offspring
½Aa
½aa

Fig. 30.—Behaviour of the chromosomes when a back-cross is made between a hybrid and one of its parents.

the black chromosome or the white. As the second maturation division, which is an ordinary cell division, does not alter the chromosome constitution, the final result is that there are two kinds of sex cells, one of which in regard to coat colour bears only a chromosome for black, the other only a chromosome for white. In other words, so far as coat colour is concerned, the gametes are pure in character (Fig. 28, c and d). The hybrid F_1 individuals of both sexes, therefore, produce two kinds of gametes.

Now since two such hybrid parents produce, in this manner, two sorts of gametes, there will be four combinations possible when fertilization takes place, as is shown in Fig. 29. Two gametes each bearing a black coat chromosome may meet, or the sperm may have the black and the egg cell the white, or the reverse may be the case, or both gametes may have the white coat chromosome. If we name the black chromosome A and the white a, we have quite clearly the Mendelian segregation of the F_2 generation—1AA : 2Aa : 1aa (i.e. AA : Aa : aA : aa).

As we have seen that sex inheritance can be regarded as a Mendelian back-cross, we have illustrated a back-cross of the coat colour example described above in Fig. 30. The description already given is sufficient to explain the details.

We may summarize this section by stating that the facts of chromosome study provide us with a visible mechanism for Mendelian inheritance, if it can be demonstrated that the chromosomes are really the carriers of Mendelian factors. There is an abundance of proof to-day in support of this, the last word being the wonderful analysis of inheritance in the fruit fly *Drosophila*[1] worked out by Morgan and his colleagues. Some of the most important evidence comes, however, from the facts of sex inheritance, as we shall see in subsequent pages.

2. *The Sex Chromosomes*[2]

We can now return to the problem of sex in order to see how far chromosome studies may aid in the way of elucidation.

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[1] Morgan, Th. H., Sturtevant, A. H., Muller, H. J., Bridges, C. B., "The Mechanism of Mendelian Heredity." New York, 1916.

[2] For a general description and for literature see Schleip, W., "Geschlechtsbestimmende Ursachen im Tierreich." Ergebn. Fortschr. Zool., 3, 1913.—Correns, C., und Goldschmidt, R., "Vererbung und Bestimmung des Geschlechts." Berlin, 1918, as well as the textbooks of Heredity previously mentioned.

The connection between cytology and sex determination was established through the important discoveries in regard to the accessory or X chromosome. The first decisive observations in this field were made by Henking, but their real significance from the point of view of our problem was first correctly understood by McClung. His interpretation required some correction, however, a service performed by Miss Stevens and above all by E. B. Wilson. Now from what we have learnt here of the chromosomes and their history it is evident that they should only occur in even numbers in the ordinary cells. The possibility of halving in the reduction division, as well as the pairing of synapsis, demands an even number. The facts now to be studied are based upon the, at first, extraordinary discovery that in the cells of many insects an odd number of chromosomes is actually present. After many errors and difficulties of investigation it can now be stated that where this is the case it is usually the male sex in which the odd number is found and then the number is always one less than is present in the female. Thus, if the latter possessed twenty-two chromosomes in the body cells, the male would have twenty-one. But we have already seen that the chromosomes are really paired, the elements of a pair being of a similar nature except that one is paternal in origin and the other maternal. Consequently in the male one chromosome, the X chromosome, must lack a partner which is present in the female with its even number. The latter sex must have two X chromosomes in addition to its other chromosomes.

In Fig. 31, a, the chromosomes of a karyokinetic figure in a bug (*Anasa tristis*) are shown, the specimen being of the male sex. In Fig. 31, b, these chromosomes are depicted individually so that they may be more easily seen, and one recognizes that there are twenty-one, of which twenty are present in pairs whilst the twenty-first lacks a partner and is the X chromosome.

In Fig. 31, c and d, the chromosomes of a cell from the female sex of this insect are similarly depicted, and one recognizes 11 pairs, both of the left-hand ones in d being the X chromosomes. Now it will be remembered that, in the reduction division of maturation, the chromosomes which had previously united in pairs were separated as entire chromosomes to the two poles of the cell, so that each daughter cell possessed half the normal number, but at the same time a complete set in which each kind of chromosome is represented. If this takes place in the female bug, each cell resulting (i.e. the egg and the polar body) will contain the like chromosome elements, that is, all the mature eggs will possess eleven chromosomes. In the male sex, however, when the maturation divisions take place and the chromosomes pair in the synapsis stage, the X chromosome having no partner must remain unpaired. Then when the reduction division takes place and the chromosomes are separated, it is forced to go to one pole (Fig. 31, f, illustrates this division and shows how the X element (h) passes undivided to one pole). The result is that two different kinds of sperm cells are produced, some with ten chromosomes (Fig. 31, g) and some with eleven, the additional one being the X chromosome. It will now be clear what must

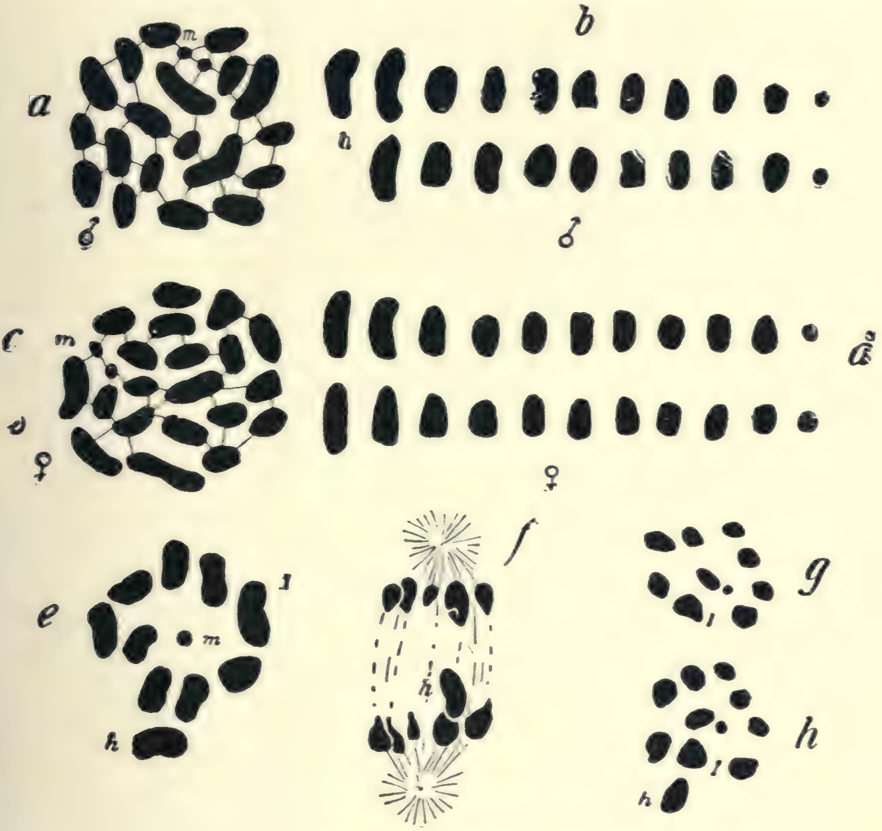

Fig. 31.—Chromosome conditions in *Anasa tristis*.

a, the chromosome garniture of the primordial sperm cells; b, the same chromosomes arranged in pairs; c, the garniture of a primordial egg cell; d, the same arranged in pairs; e, metaphase of the first spermatocyte division; f, the second maturation division; g and h, the two daughter groups of a division figure seen from the pole; h alone possesses the unpaired chromosome h.

After Wilson from Haecker.

happen when fertilization occurs; either a spermatozoon with ten chromosomes fertilizes the egg (which always contains eleven) or else a spermatozoon with eleven chromosomes performs the function.

In the first case the resulting organism will have twenty-one chromosomes in its cells, in the latter the normal number will be twenty-two. But since the males always have twenty-one chromosomes and the females twenty-two, it is apparent that the spermatozoon with one X chromosome is a female determinant, whilst the other kind without an X chromosome at all is a male-determining sperm cell.

The insects are and have been classic objects for the study of the sex chromosomes, but technical difficulties in this group often render it almost impossible to follow the complete cycle of the X chromosome through fertilization and development. Another example may therefore be described here—the chromosome cycle in the Nematode, *Ancyracanthus cystidicola*—in which, thanks to the work of Mulsow,[1] the complete history is very thoroughly and satisfactorily known. Fig. 32 illustrates diagrammatically the chromosome cycle of this worm.

The right-hand circle represents the female cycle, the left-hand one the male, and both circles touch at the fertilization point. Stage 1 on the right-hand side is the female worm with one of the primordial egg cells in the ovary containing twelve chromosomes. The two X chromosomes, which are not really distinguishable, are coloured red. Stage 2 is the egg cell alone before the period of growth. Between stages 2 and 3 synapsis takes place and the chromosomes pair; stage 3 represents the egg during the growth period when the chromosomes are not visible. They appear again united in pairs in stage 4 at the beginning of maturation, and of course there are six double elements or pairs. The first maturation division (stage 5) removes six entire chromosomes in the first polar body, whilst the second maturation division (stage 6) splits each remaining chromosome along its length and separates the halves. The mature egg is shown in Fig. 32, stage 7, with the reduced number of chromosomes, one of which is the X chromosome. This applies to all the eggs.

The male animal (Fig. 32, left-hand side, stage 1) possesses only eleven chromosomes in the primordial germ cells of its testis, one of which is an unpaired X element (cf. stage 2 this side with stage 2 of the right-hand circle). When these chromosomes conjugate in the synapsis stage the red coloured X chromosome has no partner and remains unpaired (stages 3 and 4). Its special nature is further indicated by the fact that it remains distinctly apart in the resting nucleus of the stage 3. For the first maturation division there are consequently five double elements (pairs of chromosomes) and the solitary X element. The result is that when the chromosomes are distributed to the two daughter cells (stage 5) the X element wanders undivided to one or the other and its special nature is again indicated by its aloof position in the spindle. This division gives the two primary spermatocytes, one of which will have five chromosomes, the other six (5 ordinary + 1 X chromosome). The second maturation division divides each of these cells into two by ordinary mitosis and consequently there result four spermatids, two with five chromosomes and two with six.

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[1] Mulsow, W., "Der Chromosomenzyklus bei Ancyracanthus cystidicola." Arch. Zellf., 9, 1912.

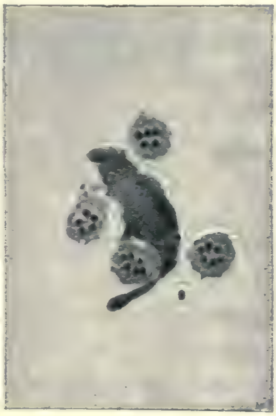


FIG. 33.—The four spermatids (still attached to the cytophore) resulting from the maturation divisions, in *Ancyracanthus*.

In this particularly beautiful example, the four spermatids remain united to a certain extent by a cytophore, and in this condition they can be isolated and serve for the production of such a convincing microphotograph as that given in Fig. 33.

Since this example has also the further advantage that the spermatid undergoes scarcely any further change before it becomes a spermatozoon capable of fertilizing a mature egg, and that during this time the chromosomes also remain visible within it, it is actually possible to observe the fundamental fact that half the eggs are fertilized by spermatozoa with six chromosomes (stage 8a) whilst the other half are fertilized by those with only five (stage 8b). The fertilized eggs will thus possess either twelve chromosomes, viz. (5 + X) + (5 + X), or eleven (5 + X) + 5 (see stages 9, 10, and 11), giving the female (right-hand side) and the male respectively. As a very distinct germ tract exists in the Nematoda, the sex cells with their chromosomes in the reproductive organs being traceable division by division from the fertilized egg cell, the complete cycle of the chromosomes is thus known.

These facts serve to show the extraordinary importance of the discovery of the sex chromosome. They indicate that a visible difference exists between the chromosome complement of the two sexes, and further that an elementary mechanism determines that the same difference will always be reproduced. In addition to this, however, they show that it is possible to see a difference in the chromosome complement which was postulated as a result of experimental breeding, namely, that so far as the sex chromosome is concerned one sex is homogametic, producing only one kind of gametes, whilst the other is heterogametic, producing two kinds of gametes.

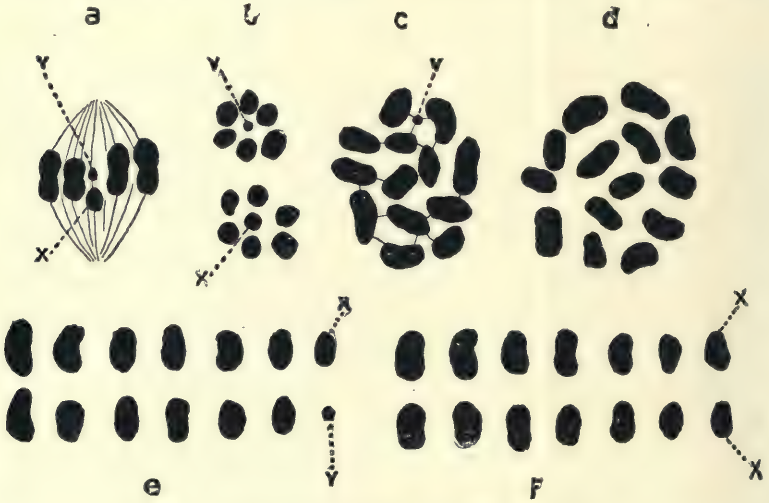


FIG. 34.—Chromosome garniture of the bug *Lygæus*.

e, the male; f, the female garniture; a, the chromosomes during the first maturation division of the spermatocyte; b, the two daughter groups of chromosomes resulting from the first maturation division; c and d, the garniture of the ♂ and ♀ cells in natural position.

After Wilson.

If we now bring this into conjunction with the conception of sex inheritance as a Mendelian back-cross, and the interpretation of the chromosomes as carriers of Mendelian characters, we at once arrive at a simple solution of the problem of the mechanism of sex inheritance. But this is anticipating.

Out of the abundance of sex chromosome investigations we have become acquainted with numerous variations of the conditions described above, and it is not the aim of this work to detail them here. Common to all, however, we find that one sex is homogametic and the other heterogametic. But the heterogametism is not always expressed in the same way. In many cases the X chromosome, that was unpaired in our example, has a partner which is distinguishable from it by a difference in form or size. It is termed a Y chromosome and the pair is spoken of as an XY group. Details of behaviour are similar to those we have already discussed—the only difference is that a Y chromosome is present where no sex chromosome was represented at all. Fig. 34 is a diagram of the typical chromosome groups of a bug which possesses such an XY group in the heterogametic sex. There are other cases again where the X chromosome is not a single element but is represented by two, three, four or even more chromosomes. The relations of such chromosome groups in division is shown diagrammatically in Fig. 35.

Although the facts we have given suffice to make evident the significance of the sex chromosomes, one might ask for further evidence that the visible chromosome differences are related to the distribution of the two sexes. Such evidence is forthcoming, some of it being overwhelming in character. Perhaps the most important point is the following: We have learnt from breeding experiments that many forms (the plant Bryony, for example) are heterogametic in the male sex and homogametic in the female, whilst in other cases (the currant moth *Abraxas*, for example) the female sex is heterogametic. If the theory of the sex chromosomes is correct, this should be demonstrable cytologically.

Breeding experiments show that in the insect groups Hemiptera and Diptera the males are heterogametic, whilst in the Lepidoptera (at least in the Geometridæ and Bombycidæ) the females are heterogametic. The mammals appear to be a group in which the males are heterogametic, whilst the birds present the opposite condition. Compare the chromosome investigations with this; in the Hemiptera we have already studied examples in which the males were seen to be heterogametic and in the Diptera and Mammalia the cytological observations agree with the above experimental breeding results. It is of extraordinary importance then to find that in the Lepidoptera, where breeding experiments have shown that the females are heterogametic, the cytological results lead to the same conclusion.

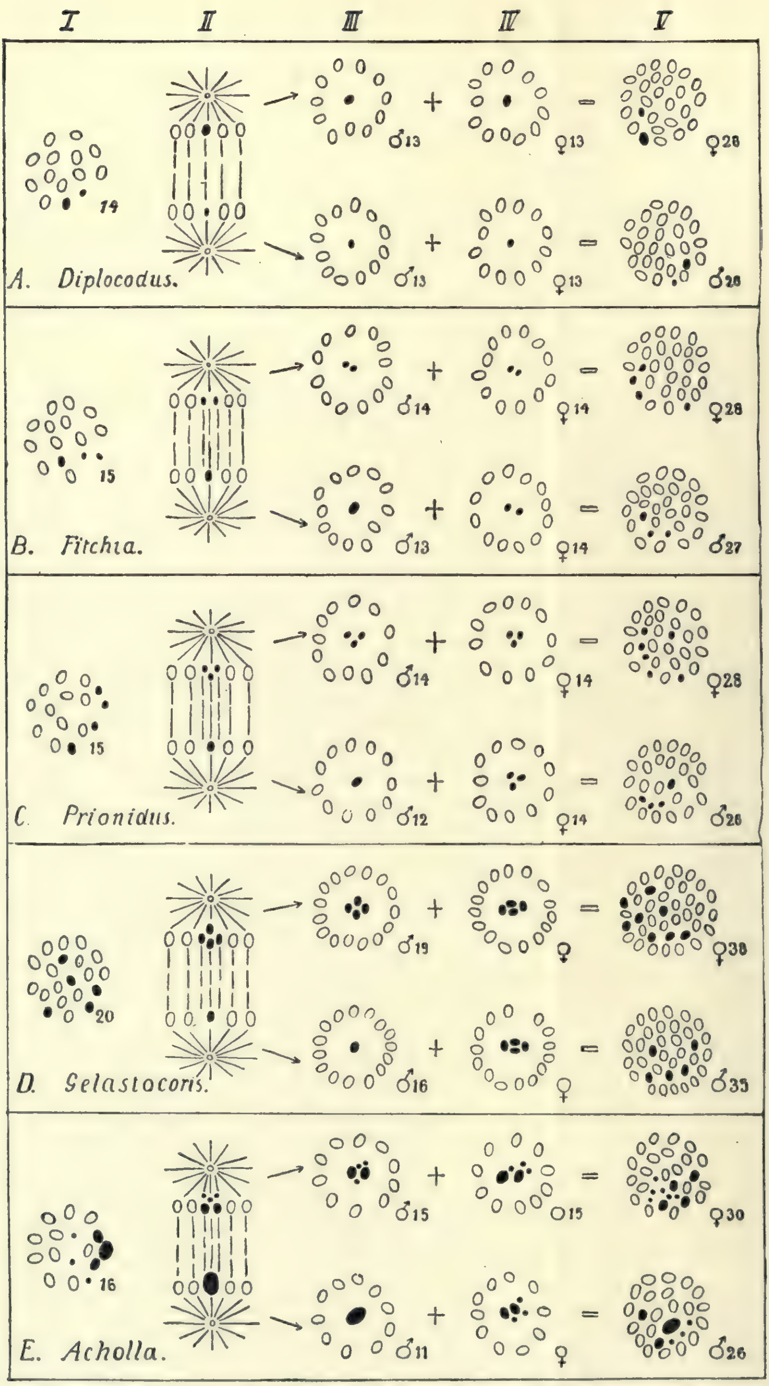

I
II
III
IV
V
14
♂13
♀13
♀28
♂13
♀13
♂26
A. Diplocodus.
15
♂14
♀14
♀28
♂13
♀14
♂27
B. Fitchia.
15
♂14
♀14
♀28
♂12
♀14
♂26
C. Prionidus.
20
♂19
♀
♀38
♂16
♀
♂35
D. Gelastocoris.
16
♂15
O15
♀30
♂11
♀
♂26
E. Acholla.

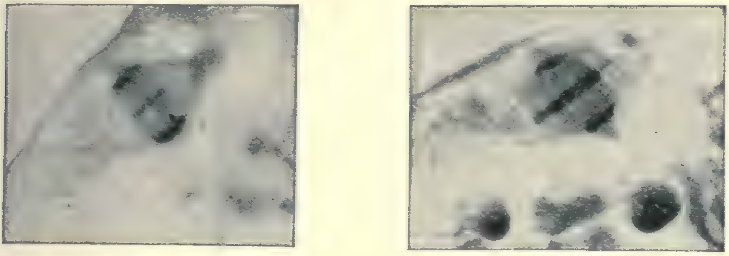
Fig. 35.—Five different types, as regards the behaviour of the sex chromosomes (indicated in black) in bugs.

Column I., ♂ cells before synapsis. Column II., the reduction division in the male. Column III., the two sorts of sperm cells. Column IV., the egg cells (one sort only). Column V., the resulting individuals.

After Payne,

Seiler[1] was able to demonstrate this for *Phragmatobia fuliginosa* (an Arctiid) and since then also particularly clearly in the Psychidæ. Fig. 36 is a microphotograph of a maturation spindle in the egg of a Psychid, *Talæporia.* Fig. 36, a, illustrates the X chromosome remaining in the egg, whilst in Fig. 36, b, it is seen passing into the polar body. Doncaster[2] also discovered a race of *Abraxas* in which the chromosome number for the female was fifty-five whilst in the male it was fifty-six. In the case of the birds no complete demonstration of the conditions has yet been given, but the facts known so far are not contradictory to the theory (Guyer).[3]

A second very important question is whether the principle is applicable to the complicated sexual conditions of hermaphroditism or to the alternation of different kinds of reproductive methods. And it is exactly in these important cases that the theory has withstood the most searching tests. Amongst other examples reference may be made to the plant louse (Aphis), the vine Aphis (Phylloxera), and the Nematode worm *Angiostomum nigrovenosum.* In the Aphids, or greenflies, a number of parthenogenetic generations, consisting exclusively of females, follow one another for some time, and then suddenly males and females are produced. From the resulting fertilized eggs only



a *b*

Fig. 36.—Maturation spindle in the egg of *Talæporia tubulosa.*

In a the X chromosome remains in the egg, in b it passes into the polar body.

Microphotograph by Dr. J. Seiler.

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[1] Seiler, J., "Das Verhalten der Geschlechtschromosomen bei Lepidopteren." Arch. Z. Zellforsch., XIII., 1914.—"Geschlechtschromosomen-untersuchungen an Psychiden." Zeitschr. f. ind. Abst. u. Vererbungslehre, XVIII., 1917.

[2] Doncaster, L., "On the Relations between Chromosomes," etc. Journ. Genet., 4, 1914.

[3] Guyer, M., "Studies on the Chromosomes of the Common Fowl as seen in Testes and Embryos." Biol. Bull., 31, 1916.

females develop, and then another series of parthenogenetic female generations follows as before. Now this cycle is accompanied by a parallel series of stages in the nucleus of the sex cells. The first fact to be noted is that the number of chromosomes is not the same in the male and female animals;[1] thus in the case of *Aphis saliceti* the female has six and the male has five for the typical number (see Fig. 37). The reduced number in the female sex cells will, therefore, be three, but there must be two kinds of male sex cells, those with three chromosomes and those with only two (Fig. 37, 2-4). Fertilization should result in half the eggs giving females (3 + 3 chromosomes) and half giving males (3 + 2 chromosomes). Actually, however, only females with six chromosomes appear out of the fertilized eggs. The history of the spermatozoa supplies the reason for this unexpected result. In the first maturation division the normal separation of the chromosomes occurs, so that one daughter cell receives three and the other two, but the latter, which ought to give rise to the male determining spermatozoa, is smaller in size from the beginning, and eventually dies (Fig. 37, 5 and Fig. 38). This of course results in there being only one kind of spermatozoa after all, and as these are female determining sperm cells, only females arise from the fertilized eggs.

The fact that parthenogenetic eggs only develop as a rule into females is explained cytologically by the absence of a reduction division and so the female chromosome number is retained. It is more difficult to explain how the so-called sexuiparous individuals of both sexes can arise from unfertilized eggs. It appears that such eggs develop with either the male or female number of chromosomes, consequently in the male eggs one chromosome must disappear at or before the commencement of development. How this happens has not been demonstrated in the case of Aphids, but evidence is forthcoming from a Phylloxeran. In this case, when the parthenogenetic egg that will produce a male is separating its polar body, one chromosome passes into it entire, so that instead of six chromosomes remaining in the egg (the division was of the normal type with splitting of the chromosomes) only five (the male number) remain (Fig. 37, ♂ *sexuipare* and ♂ egg). Thus once again the cytological facts agree excellently with the principle which has been deduced.

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[1] Morgan, T. H., "A Biological and Cytological Study of Sex Determination in Phylloxerans and Aphids." Journ. Exp. Zool., 7, 1909.—v. Baehr, W. B., "Die Oogenese bei einigen viviparen Aphiden und die Spermatogenese von Aphis saliceti." Arch. Zellf., III., 1909.

The Nematode worm, *Angiostomum nigrovenosum*,[1] is another case where the same agreement is found. Here the life cycle consists in the alternation of a free living dioecious form (a stage with separate sexes) with a parasitic hermaphrodite form. The fertilized eggs of the free living worms always develop into the parasitic hermaphrodite form and the eggs of the latter into the free living separate sexes. Cytological investigation shows that the females of the separate sex generation possess twelve chromosomes, which are reduced to six during maturation. The males of this generation have eleven chromosomes, so that spermatozoa with six and spermatozoa with five chromosomes are produced. But the hermaphrodite generation always has twelve chromosomes, consequently the spermatozoa which possessed five chromosomes must have been incapable of fertilizing the egg. The hermaphrodites possess the female number of chromosomes and are also female in external appearance. Their eggs, after maturation has taken place, have six chromosomes. In the primordial sperm cells there is also the female number of chromosomes, but one of them already presents certain peculiarities and is condemned to death. It actually survives the maturation divisions and comes into half the spermatids formed, but it is left outside the nucleus and disappears. The result is there are again two kinds of spermatozoa, some with six and some with

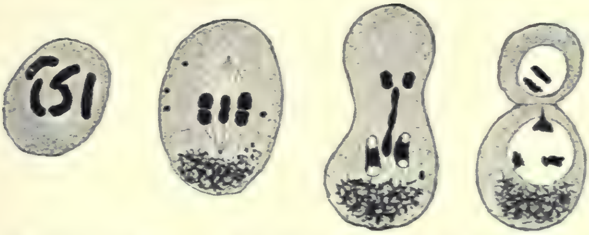

FIG. 38.—Maturation division in the spermatogenesis of an Aphid, with formation of a ♀ determining spermatid (large cell with three chromosomes) and a rudimentary ♂ determining spermatid. After V. Baehr.

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[1] Schleip, W., "Das Verhalten des Chromatins bei Angiostomum (Rhabdonema) nigrovenosum." Arch. Zellf., VII., 1911.—Boveri, Th., "Über das Verhalten der Geschlechtschromosomen bei Hermaphroditismus." Verh. phys. med. Ges. Würzburg, 41, 1911.

five chromosomes. Eggs fertilized by the former become females, those fertilized by the latter become males (see Fig. 39).

In describing these last cases we have not referred to many details; the problems of parthenogenesis and hermaphroditism do not interest us here—we shall come to them later. It is sufficient at this stage to show how the condition of the sex chromosomes always agrees with the expectations we must entertain if these chromosomes were to embody the mechanism of sex determination. The complete significance of these facts is, however, only forthcoming when they are brought into their correct relationship to the results of breeding experiments. This important step will form the subject of the next section.

d. The Identity of the Experimental and Cytological Facts

In the preceding section, dealing with the fundamental facts of the sex chromosome theory, we have intentionally expressed ourselves in a way that would lead the attentive reader independently to arrive at the conclusion that will be drawn in this chapter. If the chromosomes be the carriers of substances that we denote symbolically as Mendelian factors, it must be apparent that with several factors in the same chromosome there must be some correlation in their inheritance; in other words, they should travel together and come together to the same destination. This expectation has been brilliantly established, particularly in Morgan's *Drosophila* experiments. Applying this to the chromosomes bearing the sex factors, we should expect to find that any other factors carried by them would be distributed in the same manner as the sex factors and consequently follow the distribution of the sexes. This coupling of a character with the distribution of the sexes we have called sex linked inheritance, and we have already studied the Mendelian explanation. We shall now see that this feature is clearly explained if we assume that factors, which are sex linked in their inheritance, are situated in the sex chromosomes. A number of investigators arrived at this conclusion about the same time, amongst whom may be mentioned Spillman on the ground of theoretical considerations, Gulick as the result of chromosome studies on Nematoda, Morgan as the result of his work on sex linked inheritance in *Drosophila*, and the author on the ground of investigations into the inheritance of secondary sex characters. But the greatest volume of evidence for the correctness of this theory has been supplied by the surprisingly extensive studies of Morgan and his colleagues on *Drosophila.* For this reason instead of taking the details from the previously described *Abraxas* case, we shall utilize Morgan's material.

The reader may be reminded that in the fly *Drosophila* the male sex is heterogametic, and the cells possess both an X and a Y chromosome (Fig. 40). Morgan's original case was the following: In a normal brood of these flies a male appeared with unpigmented white eyes. A change of this kind is usually termed a mutation in heredity studies. When this male was paired with his normal red-eyed sisters, the resulting F_1 generation were all red eyed, both sexes being present. In the F_2 generation resulting from the pairing of two of the F_1 hybrids there were produced 2459 red-eyed females, 1011 red-eyed males, and 782 white-eyed males. Thus white-eyed females were totally absent. The case bears a similarity to the *Abraxas* crossing already described, except that maleness and femaleness have changed places, showing that the male sex is the heterogametic one in *Drosophila.*

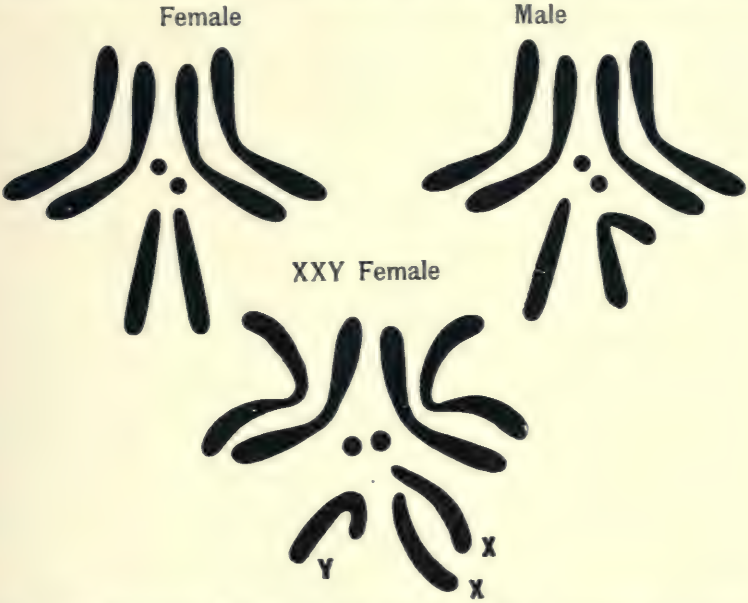


FIG. 40.—Chromosomes of the female and male *Drosophila* (somewhat diagrammatic). After Morgan.

When the white-eyed male is paired with a red-eyed female of the F_1 generation, the offspring (exactly as in *Abraxas*) consists of all the possible combinations—in one result there were 129 red-eyed females, 132 red-eyed males, 88 white-eyed females, and 86 white-eyed males.

Finally, if a wild red-eyed male is crossed with a white-eyed female, the offspring are half white-eyed males and half red-eyed females. Consequently the red-eyed wild males must be heterozygotic for white, just as in *Abraxas* the wild females were shown to be heterozygotic for the lacticolor character.

The Mendelian explanation is therefore the same for the two cases, except that the sexes are changed.

Now let us examine the chromosome conditions which are diagrammatically set out in Fig. 41. The parents in the first row are the red-eyed female and the white-eyed male, and at the side of each the sex chromosomes are shown, the female having two X chromosomes both with the pigment factor for the eye colour (and therefore depicted in black), whilst the male has one X and one Y chromosome neither having any pigment factor. The female produces eggs all of which are alike with one X chromosome bearing the factor for pigmentation (for brevity it will be termed the black chromosome); the male produces two kinds of spermatozoa, some of which have an X and some a Y chromosome, both of which are naturally white. The different possible combinations in fertilization are shown, resulting in the red males and red females of the F_1 generation. An egg with a black chromosome can be fertilized either by a sperm with a white X chromosome or by one with a white Y chromosome. In the former case a female results with two X chromosomes, in the latter a male with one X and one Y chromosome, and since redness dominates over whiteness all the F_1 generation must be red-eyed.

The F_1 hybrid females produce, however, two kinds of eggs, some with a black and some with a white X chromosome. The hybrid males produce similarly two kinds of sperm cells, some with a black X chromosome and some with a white Y chromosome. There are four possible combinations of these germ cells, as shown in the illustration, giving red-eyed females with two black X chromosomes, red-eyed females with one black and one white X chromosome, red-eyed males with one black X chromosome and one white Y chromosome, and lastly white-eyed males with a white X and a white Y chromosome. It will be seen therefore (and the same applies to all manner of crosses between these forms) that the assumption that the sex-linked character lies in the sex chromosome explains the facts.

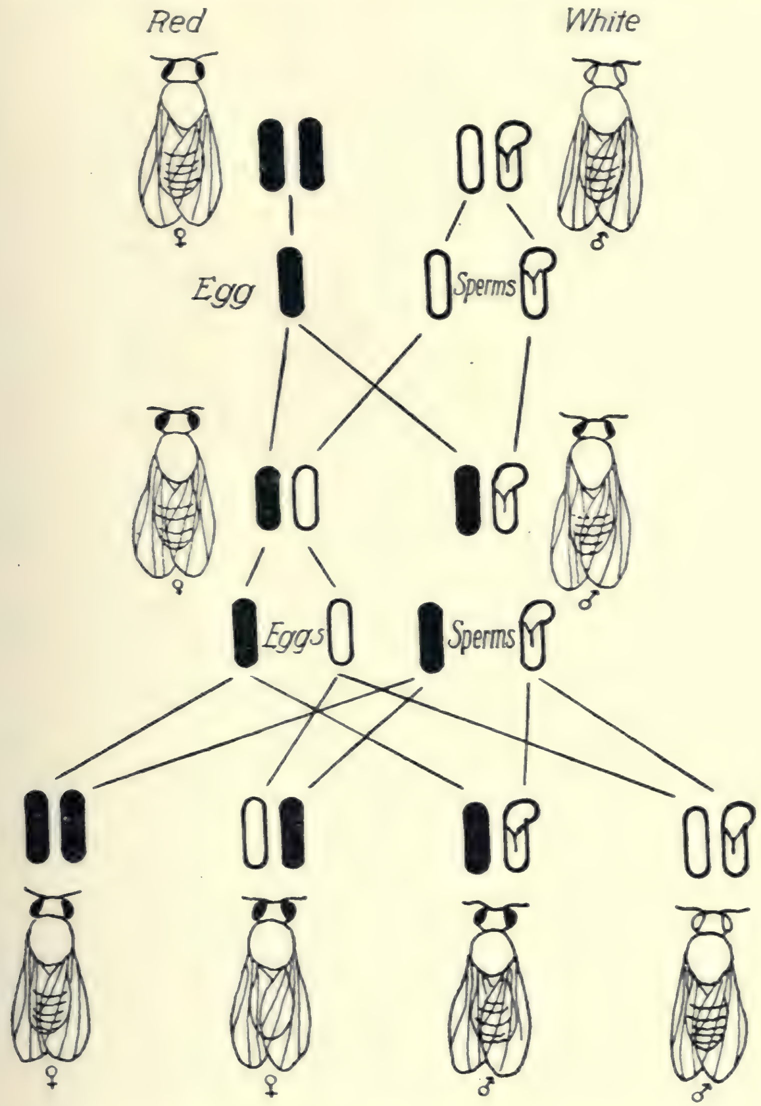


FIG. 41.

Sex-linked inheritance of white and red eyes in *Drosophila*. The black X chromosome carries the factor for red eyes, the open chromosome carries the factor for white eyes.

After Morgan.

In the *Drosophila* crosses of Morgan and his colleagues upwards of 200 new mutations have appeared whose inheritance has been studied. Quite a considerable number of these have proved to be sex linked, and in every case in a similar manner to the one already described. Moreover, if several are inherited at the same time, they are correlated together, as would be expected if the factors were all situated in the same chromosome. All kinds of mutations have appeared, in which almost every possible character of the body has been modified. Some of them are represented in Fig. 42. In a the posterior margin of the wings is "cut," in b the wing is "notched;" besides which, if the illustration were larger and printed in colours, three other sex-linked characters would be shown, namely, a peculiar condition of the body hairs, a ruby-red eye colour, and a yellow-brown body colour. Another curious feature, bound up with the last-mentioned mutations, is the fact that the flies are no longer heliotropic. When the yellow-brown males of this type and the grey females resulting from a cross are exposed to light, the females all fly to the light whilst the males do not. The fly c presents the character of rudimentary wings and the eyes are eosin in colour; d, in addition to an inheritable peculiarity of the wing veins, has bar

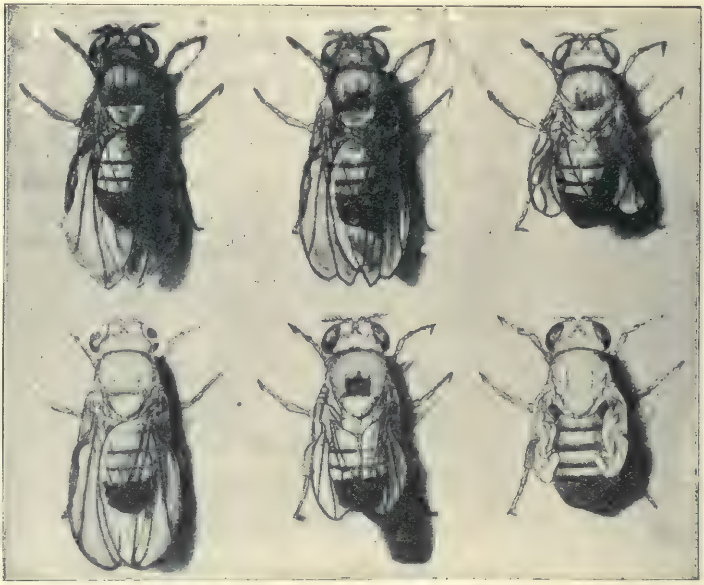


FIG. 42.—Various mutations of *Drosophila*, the factors for which lie in the X chromosome.

Upper row from left to right: "cut" wing; "notch" wing; "rudimentary" wing. Lower row: "fused" wing (the third and fourth wing veins fused) and "bar" eyed (the eye presents a band-like mutation); "miniature" wing; "pad" wing (wings not expanded). Other mutations are not clear in the non-coloured figure.

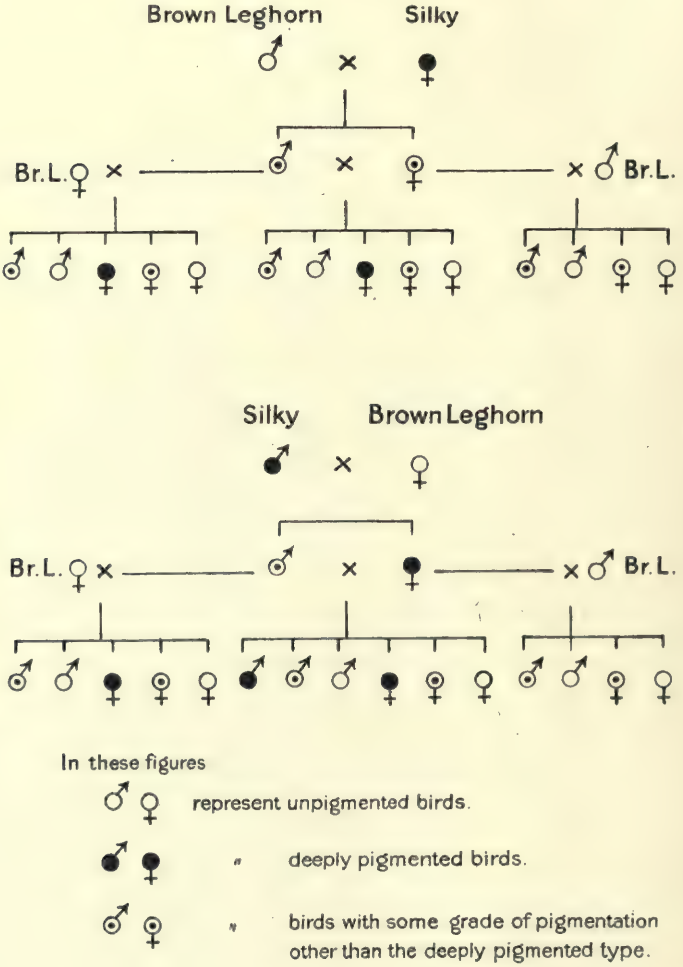
After Morgan.

eyes; e is a sex-limited mutation in which the eyes are white and the wings shortened (miniature wings); f has wings which do not unfold. These are a few of a numerous series of examples which illustrate the same principles. In other groups of animals, the birds and mammals, for example, other characters have been discovered which behave in heredity in the same way as these *Drosophila* and *Abraxas* examples. The best-known cases are the barred pattern of the Plymouth Rock hens, the coat colour in tortoise-shell cats, and certain abnormalities in man such as colour blindness and hæmophilia.

Those who are well acquainted with the details of Mendelian investigation know that numerous complications exist which have not been considered here. In some of the more important the determination of certain characters depends upon the combined action of several independent factors such as pigment intensifiers, pigment diluters, and multiple or additive factors for a character. If, for example, three different pigment factors acting together produce deep red, it is possible for the sixty-four F_2 combinations of these factors, with their recessives, to present a complete series of colours from dark red to white. Now factors of this kind are known which are either Mendelian or sex linked in their inheritance, as, for example, a factor which darkens the colour in *Drosophila* and is found in an ordinary chromosome, whilst another with a similar action lies in a sex chromosome. When this feature is combined with those described above some very remarkable cases of sex-linked inheritance result.

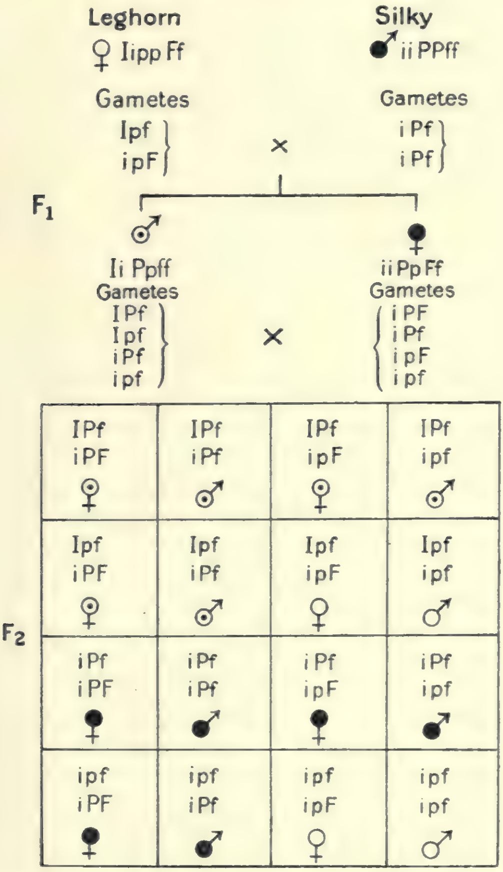
As an example of this type we append a description (from the work of Bateson and Punnett) of inheritance in the Silky fowl. One of the most remarkable features of this breed is a strong deposit of black pigment in the mesodermal tissues of the body. If the Silky fowl is crossed with the ordinary brown Leghorn, the F_1 generation differs in character according to the direction of the cross. For example, Silky ♀ × Leghorn ♂ gives weakly pigmented F_1 hybrids; but Leghorn ♀ × Silky ♂ gives F_1 hybrids, the males of which are weakly pigmented, whilst the females are deeply pigmented. In the F_2 generation all grades appear from pigmented to non-pigmented. When the back-cross is made with the brown Leghorn, there is again a difference according as to whether the male or the female parent is the F_1 hybrid. The diagrams make the details quite clear and serve better than a long description.

The sex-linked inheritance shows itself once in the F_1 cross and again in the absence of dark pigmented males in all crosses except one. The explanation given by Bateson and Punnett is the following: Pigmentation depends upon a factor for pigment P and an inhibiting factor I; and the different grades of pigmentation depend upon the composition of the zygote in regard to these two factors. Thus PPii will be deeply pigmented, ppII and ppii will be quite unpigmented, and so on. Sex determination follows according to the formula Ff = ♀ and ff = ♂, and it is supposed that P and I repel each other so that they cannot


Brown Leghorn
Silky
Br.L.
Br.L.
Silky
Brown Leghorn
Br.L.
Br.L.
In these figures
represent unpigmented birds.
" deeply pigmented birds.
" birds with some grade of pigmentation other than the deeply pigmented type.

from Bateson & Punnett

enter the same gamete. The crossing of a Leghorn female with the Silky male may now be represented by the following scheme:—


Leghorn
♀ Iipp Ff
Silky
♂ ii PPff
Gametes
Ipf
ipF
×
Gametes
i Pf
i Pf
F1
♂
Ii Ppff
♀
ii Pp Ff
Gametes
I Pf
I pf
i Pf
i pf
×
Gametes
i PF
i Pf
i pF
i pf
F2
IPf iPF ♀
IPf iPf ♂
IPf ipF ♀
IPf ipf ♂
Ipf iPF ♀
Ipf iPf ♂
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iPf ipf ♂
ipf iPF ♀
ipf iPf ♂
ipf ipF ♀
ipf ipf ♂

The results of other crosses may be deduced in the same way. Here then is an example which in some ways runs exactly like that of *Abraxas* but in other respects is complicated by the fact that a sex-linked factor I is working together with a factor P which is inherited in the ordinary way. The case is clear if we assume that the factor I lies in the X chromosome whilst P lies in another chromosome altogether.

Goldschmidt[1] has recently analysed a still more complicated case, the inheritance of Melanism in the Nun moth. All the stages of wing pigmentation, which extend from white to black, are found to be determined by the combined action of three Mendelian factors, one of which lies in the X chromosome, and the two others in autosomes. The complicated expectations which should be realized in experiments (the above being the factorial basis) can be worked out from the preceding explanations.

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[1] Goldschmidt, R., "Erblichkeitsstudien an Schmetterlingen, III." Zeit. f. indukt. Abst. Vererbgsl., 25, 1921.

It would be difficult for anyone looking impartially over the facts which have been briefly described in the preceding pages to escape the conclusion that sex-linked characters were inherited in the X chromosome, and that the Mendelian scheme of sex inheritance was a symbolic expression of the sex chromosome mechanism. The foundation for such a theory seems secure. We can go further, however, and assert that an undeniable experimental proof has been furnished, the result of the work of Bridges[1] on *Drosophila.* It will be remembered that white eye colour was a sex-linked mutation and consequently a white-eyed female crossed with a wild red-eyed male gave exclusively red-eyed females and white-eyed males (criss-cross inheritance). Now in certain crosses of this kind there appeared, in addition to the expected forms,[2] a number of unexpected individuals. Actually, together with about 47·5 per cent red females and 47·5 per cent white males, there were 2·5 per cent white females and the same per cent of red males. Whence came this 5 per cent which does not fit in with the theory?

Bridges found that one could explain this result if one assumed that an abnormality occurred during the maturation of the eggs. In the normal state of affairs one X chromosome should remain in the egg and one should pass into the polar body. It might happen that the two X chromosomes failed to disjoin and both remained in the egg or both passed into the polar body (non-disjunction of the chromosomes). If such eggs of a white-eyed female were fertilized by spermatozoa from a red-eyed male, the conditions illustrated diagrammatically in Fig. 43 would arise. Two kinds of eggs are shown, one with both X chromosomes both carrying white, the other without any X chromosomes at all. There are two kinds of spermatozoa, one kind with an X chromosome carrying red, the other with a Y chromosome. Fertilization gives four possible combinations :—

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[1] Bridges, C. B., "Non-disjunction as Proof of the Chromosome Theory of Heredity." Genetics, V. I., 1916.

[2] As a matter of fact another sex-linked mutation (vermilion) was used in the actual experiments. From the point of view of illustration this makes no difference and "white eyes" has been used instead.

1. Egg with two white-eyed X, fertilized by sperm cell with red-eyed X.
2. " " " " X, " " " " " " Y.
3. " without X, " " " " " " X.
4. " " X, " " " " " " Y.

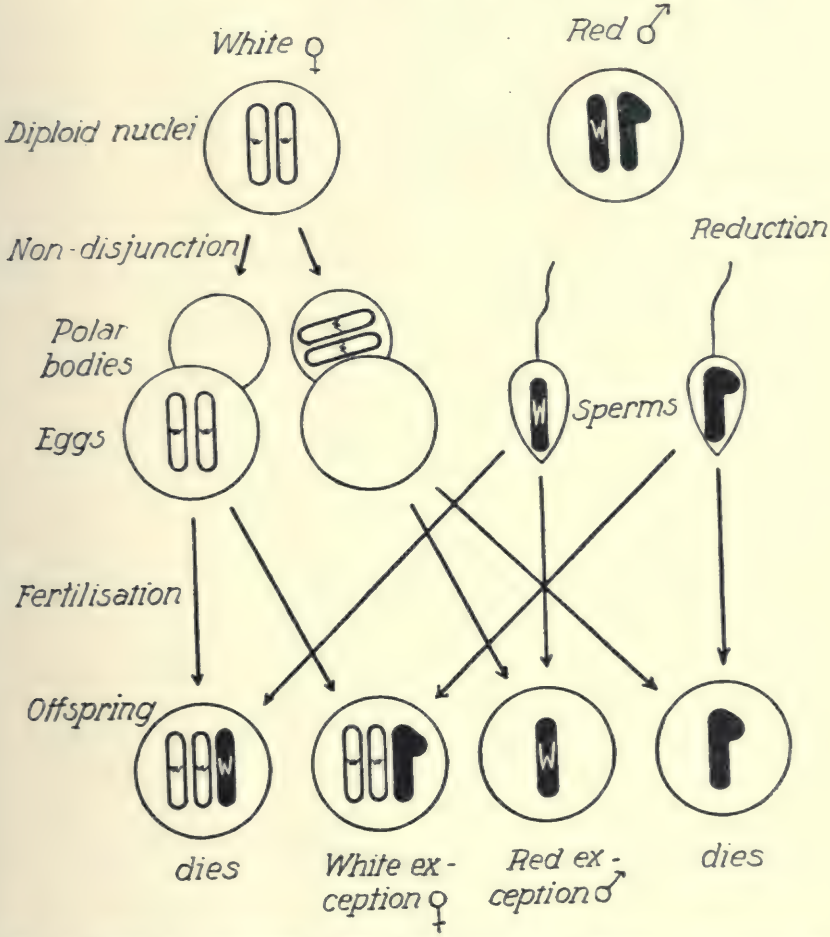
White ♀
Red ♂
Diploid nuclei
W
Non-disjunction
Reduction
Polar bodies
Eggs
W
Sperms
Fertilisation
Offspring
W
W
dies
White exception ♀
Red exception ♂
dies

FIG. 43.—Primary non-disjunction of the X chromosome in *Drosophila*. Explanation in text. After Bridges.

Number 2 would be a white-eyed female (one of the exceptional daughters) having an extra Y chromosome, and number 3 would be an exceptional son, a red-eyed male, in which the Y chromosome was missing. If it were assumed that numbers 1 and 4 were incapable of living, the breeding result referred to above would be explained. But the white-eyed females produced in this abnormal way possess two X chromosomes and a Y chromosome, whereas normal females have only two X chromosomes. Further breeding of these curious females should then give further abnormal individuals. A scheme showing certain possible combinations is depicted in Fig. 44. During the synapsis period, when the paternal and maternal chromo-

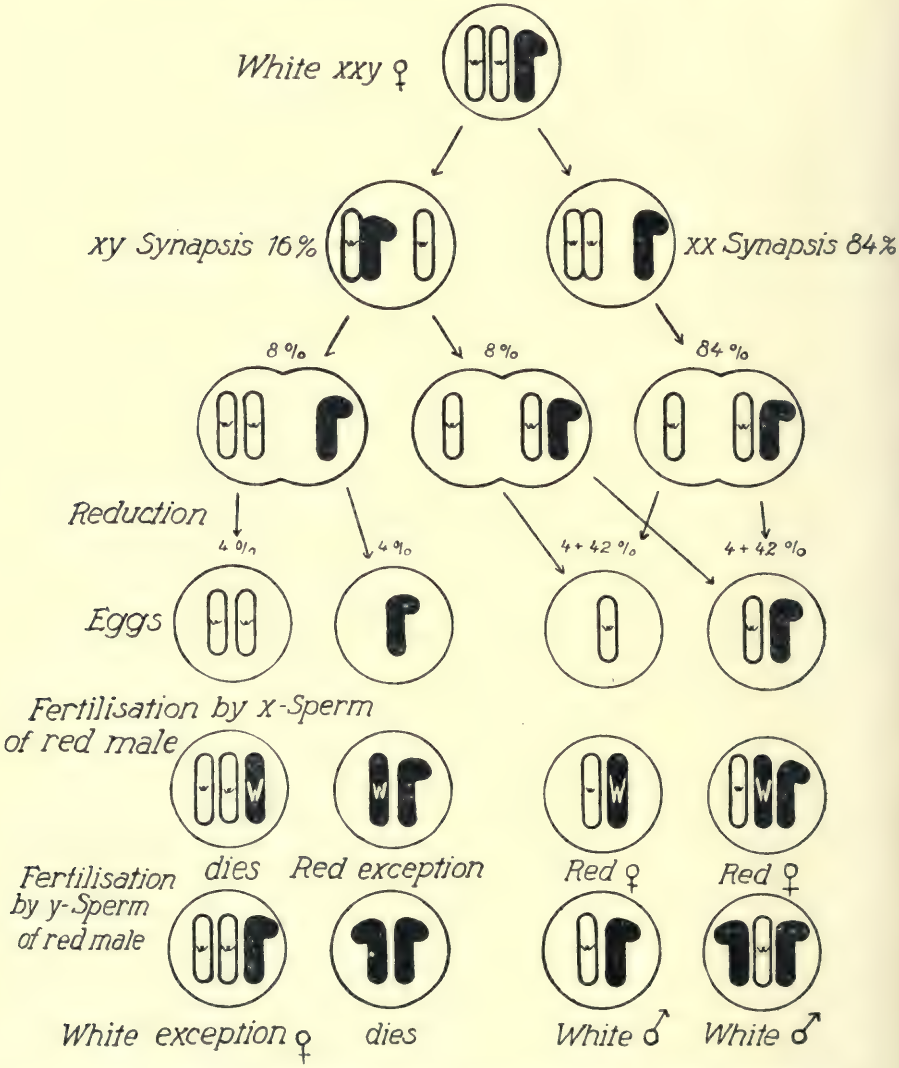
White xxy ♀
xy Synapsis 16%
xx Synapsis 84%
8 %
8 %
84 %
Reduction
4 %
4 %
4 + 42 %
4 + 42 %
Eggs
Fertilisation by x-Sperm of red male
W
W
W
W
dies
Red exception
Red ♀
Red ♀
Fertilisation by y-Sperm of red male
White exception ♀
dies
White ♂
White ♂

FIG. 44.—Secondary non-disjunction of the X chromosome in a female of *Drosophila*. Explanation in text. After Bridges.

somes pair, the two X chromosomes might pair or one of them might conjugate with the Y chromosome, leaving the other apart. In only about 16 per cent of cases does the XY conjugation occur. The result would be that the reduction division would give *four* kinds of eggs, as the figure shows, some with two X chromosomes, some with only one X, some with only a Y chromosome, and others with both X and Y chromosomes. In every case, however, the X chromosome would be carrying the white-eyed character. Now if these eggs are fertilized with the spermatozoa from a wild male, half of which bear an X chromosome with red-eyed character and half a Y chromosome, there should be eight possible combinations, viz. :—

1. Two white-eye X chromosomes and a red-eye X chromosome
2. A Y and a red X chromosome = ♂
3. A white X chromosome and a red X chromosome = ♀
4. „ X „ „ X „ and a Y chromosome = ♀
5. Two white X chromosomes and a Y chromosome = ♀
6. „ Y chromosomes
7. A white X chromosome and a Y chromosome = ♂
8. ,, X ,, ,, two Y chromosomes = ♂

Of these combinations numbers 3 and 4 must be red-eyed females, numbers 7 and 8 white-eyed males, number 5 white-eyed females, and number 2 red-eyed males. Numbers 1 and 6 have never been found; they are supposed to die owing to their abnormal constitution. The females of type 5 would again produce four kinds of eggs in the next generation, and so on. The numerical relationships of the different classes to one another—the abnormal and unexpected to the normal—naturally depends on the frequency of the different types of synapsis. These are the main points in Bridges' explanation embodying the theory of non-disjunction of the X chromosome pair in the egg.

The proof of the accuracy of Bridges' theory lies first in the fact that the unexpected white-eyed females of the supposed constitution XXY gave the same abnormal results after fertilization with red-eyed males. This was indeed always the case. Then, on the other hand, the unexpected red-eyed males of the experiment should behave like normal males, for they have the same factorial constitution. This also has been demonstrated. There should be two types, however, of the red-eyed females (those numbered 3 and 4 in the diagram), of which one (3) is normal and heterozygotic for redness, whilst the other has the abnormal chromosome constitution. One can calculate the results of crosses with these two females, and the actual experimental results again agree with the theory. The same applies to other crosses, the experimental results agree with those calculated on paper. There are also two kinds of white-eyed males, namely, numbers 7 and 8 of the table. The first is quite normal and should give corresponding results. The second has two Y chromosomes and can therefore produce sperm cells with the constitution XY. If these fertilize an egg containing an X chromosome, females with the constitution XXY will be produced, and these are once again females which will give the exceptional classes when reproduction takes place. The decisive proof, however, would be cytological evidence that the females which ought from their behaviour in breeding to possess the constitution XXY actually produce sex cells with two X chromosomes and one Y chromosome. This has been demonstrated. Fig. 40 (p. 61) is an illustration of the normal chromosome constitution of Drosophila, and Fig. 45 shows two chromosome groups from XXYY and XXY females respectively. *We consider this striking investigation the keystone of the study of the mechanism of sex inheritance. The evidence stands on the same level as a demonstration in experimental physics.*

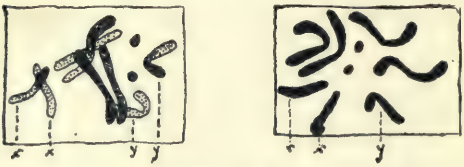

FIG. 45.—Chromosomes of XXYY and XXY individuals of *Drosophila*.
After Bridges.

e. Appendix. Polyembryony and the Distribution of the Sexes

The biological facts in regard to twins and Polyembryony should be added to the evidence brought forward to explain the mechanism of sex distribution.

In certain animal groups a remarkable feature of development is the division of the embryo at a very early stage into several parts, each of which becomes a complete embryo. Thus in the Armadillo *Dasyurus novemcinctus* four embryos originate from one egg, in *D. hybridus* the number is larger and variable.[1] In the case of certain wasps (Chalcididæ), the eggs of which develop parasitically within the eggs of Lepidoptera, a similar process takes place, resulting sometimes in several hundred individuals from one fertilized egg.[1] In each of these examples all the individuals arising from one egg are of the same sex, as is required by the theory set out above.

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[1] A summary of the facts is given by Newmann, H. H., "The Biology of Twins." Chicago, 1917.

f. Summary and Conclusions

The results of the preceding discussion can now be summarized as follows : The normal distribution of the sex to the offspring necessitates the presence of some regulating mechanism. Experiments in heredity have shown that this mechanism has the character of a Mendelian back-cross in which one sex is always heterozygotic, the other homozygotic, for a sex factor. The first produces two kinds of gametes, in other words is heterogametic ; the other produces only one kind, it is homogametic. The inheritance of sex depends then on an alternative mechanism which so acts that always one sex produces two kinds of gametes.

Now such a mechanism is visibly given in the characteristic manner of distribution of the sex chromosomes during the maturation of the sex cells, and consequently these structures may be regarded as the carriers of the controlling substances, the sex factors. If any other inheritable factors come into the range of this mechanism, they are carried along by it and their inheritance is sex linked. If we wish to regard such cases in the terminology of Mendelism, we must introduce into our customary mode of treatment of the Mendelian factors mechanisms working on analogous lines to the chromosome mechanism—such as the assumptions of factor repulsion, coupling, and sex-limited dominance.

Yet this is after all only a form in which we give expression symbolically to mechanisms which are rendered visible in chromosome distribution. The Mendelian interpretation and the chromosome data are therefore the same things stated in different terms. The mechanism for the normal distribution of the sexes is thus completely explained.

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[1] Marchal, E., "Recherches sur la biologie et le développement des Hymenoptères parasites." Arch. zool. exp. gén., 1904. Further works by Silvestri, Hegner, Patterson.

CHAPTER III

THE PHYSIOLOGY OF SEX INHERITANCE

UP to this point we have only concerned ourselves with the mechanism which distributes that upon which the actual differentiation of the sexes depends. If we were to compare our problem with the organization of a railway station, we should have studied only the tracks and systems of points, which of course are responsible for the proper passage of the trains. We have not yet considered how the trains are made up nor the power that moves them. We must now advance a step further and take up the next question—what is actually distributed by the mechanism, and in what manner does it bring about sex differentiation?

a. Sex Factors

We have already made the assumption in the preceding chapter that the substances distributed and transmitted by the mechanism are some kind of Mendelian factors. And as a matter of fact the view generally accepted to-day is that the determination of sex depends upon a pair of Mendelian factors. This, however, is a general statement, and if we attempt to go further into detail we find more difficulties in the way of explanation than at first might be expected.

If the most simple standpoint is taken (that of the rather early days of Mendelism) and we regard a factor as the carrier of the *anlage* of one very definite character, then a sex factor must be the carrier of the *anlage* for femaleness or maleness. Let us see where this conception will lead us. If we adopt the Mendelian formulæ Mm = ♂ and mm = ♀ for sex inheritance, the X chromosome of the male must be the carrier of the factor for maleness. But we have seen that the spermatozoa which possess the X chromosome are female determiners, and consequently the females must also have an M. This, however, is not given by the formula. Another way out of the difficulty has been tried and, since in this instance the female possesses two X chromosomes and the male only one, the female must have two determining factors and the male one. But this can only be the female factor F, so the females would have the formula FF and the males Ff. The consequence of this is the assumption that the male in its X chromosome carries a female-determining factor, notwithstanding which it is a male. The absence of femaleness must be dominant over its presence, so that a male results. This would be simply absurd.

Another method which has been adopted is not much more satisfactory.[1] It leaves the presence and absence theory on one side, and regards the female as a hybrid between maleness and femaleness with femaleness dominant. The female (with two X chromosomes) could then be represented as having the constitution F(M), and one X chromosome would carry the character F and the other M. The male, on the other hand, with only one X chromosome, would carry the factor for maleness, the partner of this chromosome being missing. Now the female will form two kinds of gametes, those with M and those with F—it is heterogametic. The male will also form two kinds of gametes—those with M (in the X chromosome) and those without an X chromosome. Consequently, if there is free fertilization between these gametes, four combinations must be possible, of which one would be MM in constitution, that is, a male with two X chromosomes, and another would be F, that is, a female with only one X element. Neither of these, however, are found. The only way of escaping this difficulty is to suggest the possibility of selective fertilization, to suggest that an egg with an F factor can only be fertilized by a sperm bearing the factor M, and an egg with M only by a spermatozoon without an X chromosome. Selective fertilization of this kind is very improbable; in any case it is quite unsupported by experimental evidence, and as a matter of fact the theory has not found many adherents.

We will not follow this type of explanation any further, for at the present time the simple point of view we have assumed in the preceding lines is not generally supported. In reality it is rendered *a priori* impossible by the pre-Mendelian investigations of Darwin and Weismann, which showed that each sex was capable of developing the characters of the other; the cock-feathered hen and the eunuch being examples. Each sex, therefore, must possess the fundament or *anlage* of both sexes, and the heterozygote-homozygote sex factor which is distributed on the sex chromosomes must be a sex determinant, or a sex differentiating factor which decides which of the two fundaments shall appear (a view which was first clearly pointed out by Correns).[1] The discoveries of cytology lead, however, a little further than this, for the results of chromosome studies given above, and others to be discussed later, indicate that the sex depends essentially upon the number of X chromosomes (one or two) in the fertilized egg, and that this purely quantitative condition is decisive, not the quality of that which is present in the chromosomes. This comes out most distinctly in the experiments of Bridges given in detail above. The different abnormal combinations (see Fig. 44) show that it is all the same in the end whether a sperm cell happens to be male or female-determining at fertilization. A spermatozoon with an X chromosome should really produce a female when it fertilizes an egg, but if the egg happens to be without an X chromosome the result is a male. A spermatozoon with a Y chromosome should produce a male by fertilizing an egg, but if the egg happens to contain two X chromosomes the result is a female.

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[1] For a discussion see Wilson, E. B., "Studies on Chromosomes, III." Journ. Exp. Zool., 3, 1906.—Castle, W. E., "A Mendelian View of Sex-heredity." Science, 29, 1909.

The deciding feature is then exclusively the presence of two X, or one X chromosomes, a fact which led Wilson[2] and other cytologists in the past (independent of the factor theory) to believe that it was the presence of two portions of X substance or one portion which was all important.

This short account will indicate that for the proper understanding of the nature of sex inheritance certain other questions must be answered. What kind of a process is it which determines that of the two sex fundaments present in a bisexual organism only one normally develops? How can this process be brought into line with the factorial hypothesis and the heterozygote-homozygote scheme? What rôle in this connection is played by the quantitative one X or two X chromosome mechanism? What is the physiology of the whole process?

We believe that answers of an almost completely satisfying nature can be given to these questions; answers which result from the experimental study of a phenomenon which we have termed Intersexuality. We shall discuss this in the following sections.

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[1] Correns, C., in "G. Mendel's Letters to C. Naegeli." Abh. K. Sächs. Ges. Wiss. Math.-phys., Kl. 29, 1905.

[2] Wilson, E. B., "Studies on Chromosomes, III." Journ. Exp. Zool., 3, 1906.

b. Experimental Intersexuality

For a long time it has been known that occasionally in nature, and also in breeding experiments, individuals occur which are mixed in sex. Both as regards the external so-called secondary sexual characters and the sexual organs themselves these individuals present a mixture, to a greater or less extent, of the characters of both sexes. It is possible for so many grades to occur as to form a complete series leading from one sex to the other. These interesting individuals are known as abnormalities under a variety of names, such as hermaphrodites, gynandromorphs, cock-feathered (female) birds, and so on; but usually different kinds of sex mixture involving perhaps different phenomena are indiscriminately classed together under these names.

Experimental analysis now allows us to pick out a very important group of these cases and to consider them as examples of a particular phenomenon, that of intersexuality. We believe that the study of intersexuality has gone a long way toward solving the problem of the physiology of sex determination.

1. Introductory Remarks

In order to estimate correctly the importance of intersexuality we must first clear up a point—a special part of the greater problem of determination. The results of experimental research during the past ten years have shown that two large groups are to be distinguished in the animal kingdom from the point of view of the determination of sex characters during the development of the individual.

In the first group the insects occupy a leading position, and so far as we know all that concerns sex is fixed with the event of fertilization. In other words, with the completion of fertilization it has been decided which sex with all its attributes will develop or, as we shall see later, which sex intergrade. Every cell of the body arising from the fertilized egg is *irrevocably* determined sexually, and the possibility of one part of the body being influenced by another is cut out. This conclusion can be deduced in the first place from experiments made to trace the relationship between the sexual organs and those sex attributes, the so-called secondary sexual characters, and it is supported by other work, particularly that on intersexuality.

The classic objects for the study of this type of behaviour are the Lepidoptera (especially the moths), as is clearly established by the complete agreement in the results attained by Oudemans, Kellogg, Meisenheimer, Kopeč, and Prell.[1]

Meisenheimer, who continued on a broader basis the experiments satisfactorily initiated by Oudemans, worked with the Gipsy moth, *Lymantria dispar.* In this insect, as in many others, the gonads are differentiated at an early larval stage, long before the external sexual differences, which are only visible in the winged adult, appear.

These sexual differences include a difference in size (the females are considerably larger than the males) and a difference in colour (the female's wings are white with dark ill-defined bands, whilst the wings of the male are brown).

If the sex organs of the caterpillar are destroyed, this has no effect upon the external appearance of the adult which develops therefrom ; the moths arising from castrated caterpillars present the typical secondary sex characters. The experiments were carried a step further in order to determine whether the presence of sex organs introduced from the opposite sex exerted any influence. Male caterpillars were castrated, and the operation of introducing the ovary from a female individual was successfully carried out ; the converse experiment was equally successful. It was found that the foreign sex organs developed quite normally in their artificial situation, but without exerting any influence on the secondary sexual characters. It was actually possible to obtain male moths with all their typical characteristic features, although the whole body was full of ripe eggs.

There was still perhaps the possibility that the destruction or transplantation of the sex organs had been carried out too late for any effect upon the soma. Hegner met even this objection, for he was able to destroy the sex organs in their embryonic stage—the insects have a typical "Keimbahn" (germ cell lineage) —and there was no influence on the secondary sexual characters.

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[1] Oudemans, J. Th., "Falter as kastrierten Raupen." Zool. Jahrb. (syst.), 12, 1899.—Meisenheimer, J., "Experimentelle Studien zur Soma-und Geschlechtsdifferenzierung." Jena, 1909.—Kopeč, V. L., "Untersuchungen über Kastration und Transplantation bei Schmetterlingen." Arch. Entwicklungsmech., 36, 1913.—Kellogg, V. L., "Influence of the Primary Reproductive Organs," etc. J. Exp. Zool., I., 1904.—Prell, H., "Über die Beziehungen zwischen primaren und sekundären Sexualcharakteren bei Schmetterlingen." Zool. Jahrb., 35, 1915. (Allg. Abt.).

Meisenheimer attained the same result in another way. He reproduced the early embryonic stage of a particular organ, the wings, by destroying the imaginal discs, an act which was followed by new development through regeneration. But the larva operated on had previously been castrated and supplied with new sex organs from the opposite sex. Notwithstanding this the regenerating wings always possessed the characters of those proper to the original sex. These amazing experiments show with certainty that the sex organs, and the somatic structures which are characteristic of the sex, can be completely independent of one another.

To the second group referred to belong the birds, mammals, and certain invertebrates. One of the most fascinating chapters of modern physiology is the study of internal secretions;[1] the study of the influence of secretions from glands like the hypophysis, thyroid, thymus, and the sex organs on the structure, development, and functions of the body. In this connection we may allude to the influence of the thyroid on the metamorphosis of the Amphibia,[2] or of the same organ on the development of a physically and psychically normal human being.

Now the facts show that in this group an intermediate step is interpolated in the determination of the organs and their functions. Compared with the insects this represents a higher evolutionary stage. In the Insecta every cell possesses all that is necessary for its determination, and consequently each is independent of the rest of the organism. In the group now being considered a central organ—some particular ductless gland—is present which produces the so-called hormones that are necessary for the completion of determination. We have a higher stage before us in which certain developmental processes are no longer the result of the independent activity of the individual cells, but are co-ordinated and regulated through the activity of a centre.

The two types may be compared, to use a parallel, with two states in one of which each province has its own code of laws, whilst the other is a state with central jurisdiction. Now the secondary sexual characters are attributes which may be associated with almost every part of the body. And their specific development, whether it be male or female, is regulated in this second type by an internal secretion which arises in the reproductive organs. A castration experiment similar to those made on the insects referred to above will have therefore very different results here. The cessation of the typical internal secretion will result in the disappearance of the characters peculiar to the sex concerned, whilst the transplantation of the organs of the opposite sex should result in the production of the secondary sexual characters of that sex.

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[1] Biedl, A., "Innere Sekretion" (2nd ed.). Berlin u. Wein, 1913.

[2] Gudernatch, J. F. "Feeding Experiments on Tadpoles." Arch. Entwicklungsmech., 35, 1913.

If the phenomenon of intersexuality is possible in both the groups, in the first it must be determined with fertilization, i.e. be zygotic, whilst in the second it will be dependent upon the condition of the internal secretions, in other words it will be hormonic. It is to be expected that the first group, presenting zygotic intersexuality, which is the simpler condition physiologically, will offer us a clearer insight into the phenomenon.

2. Zygotic Intersexuality

The experimental production of zygotic intersexuality and its almost complete analysis is given in our investigations[1] on *Lymantria dispar*, the Gipsy moth.

Insect breeders have known for a long time (detailed notes are given in particular by Standfuss)[2] that when species, or even geographical varieties, of Lepidoptera are crossed, sexual abnormalities frequently occur. Besides this every collector knows that similar abnormalities occasionally turn up in nature. A relatively common case of this kind is the occurrence of the so-called colour hermaphrodites of the Gipsy moth. Now this insect is characterized by a very marked difference between the two sexes, and also by a very wide geographical distribution which favours the existence of distinct local varieties. For these reasons it seemed likely to prove a suitable object for experimental work—an expectation which has been realized.

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[1] Goldschmidt, R., "Erblichkeitsstudien an Schmetterlingen, I." Ztschr. ind. Abst., 7, 1912.—*Ibid.* 11, 1914.—"Experimental Intersexuality and the Sex-problem." Amer. Nat., 50, 1916.—"A Further Contribution to the Theory of Sex." Journ. Exp. Zool., 22, 1917.—"Intersexuality and the Endocrine Aspect of Sex." Endocrinology, I., 1918.—"Untersuchungen über Intersexualität." Ztschr. ind. Abst., Bd. 23. In the Press.

[2] Standfuss, B. M., "Handbuch der paläarktischen Groszschmetterlinge." Jena, 1896.

Crosses were first carried out between European and Japanese races. The first important result, one that had already been obtained by an amateur breeder named Brake, was that whilst normal offspring arose from the cross Japanese females with European males, the reciprocal cross European females with Japanese males gave peculiar F_1 animals. The males were normal, but the females presented various mixtures of male and female characters. They were termed intersexes. From the intersexual females which were still capable of reproduction it was possible to obtain F_2 generations in which segregation took place, with the result that half the females were normal and half intersexual. But the reciprocal cross gave only normal females in the F_2 generation just as in the F_1; there might, however, be a certain percentage of males intersexual. This experiment shows clearly that both sexes are capable of developing the characters of the other when certain definite combinations of hereditary material which are not normal are brought about by crossing. Such is zygotic intersexuality. The above experiments also show that the factor or factors concerned are inherited along Mendelian lines, for we have typical segregation of intersexuality in the F_2 generation.

Further investigation brought to light another set of facts. It showed that there were many different races of European, Japanese, and American Gipsy moths which are typically distinct in regard to the factor or factors responsible for the production of intersexuality. The expression of this difference lies in the fact that the extent of intersexuality (that is to say, the degree of development of the characters of the other sex) is definite and typical for a particular cross. Crosses of this race and that give only a low grade of intersexuality, other races give a middle degree of intersexuality, whilst others again give a high degree of intersexuality. Thus one can produce every stage from a female to a male, or the reverse, in a manner predetermined. In the first members of a series of this kind the combinations must be of such a nature that they produce only normal offspring, whilst at the end the combinations convert one sex entirely into the other.

The chief data in regard to female intersexuality are as follows:[1] Let us take first the Japanese race Gifu. If males of this race are crossed with females of the Japanese race Kumamoto, all the F_1 females are slightly intersexual. The antennæ are weakly pectinate, and there is a little of the brown male pigment on the white wings, the egg production is somewhat diminished, but the copulatory organs and instincts are normal and therefore reproduction is possible. Now take this same Gifu male and cross with the Japanese race Hokkaido or the Schneidemühl European race—the F_1 females will be more pronouncedly intersexual (see Fig. 46). All the secondary sexual characters will be more male, but the instincts will be still those of the female. Fertilization is not possible although sufficient mature eggs are produced. If males of the same race again (Gifu) are crossed with females of the Fiume race, a still higher degree of intersexuality is reached amongst the females of the F_1 generation. The secondary sexual characters of these individuals are almost completely male in type, and the instincts are also affected so that they come to be something between female and male in nature. Copulation does not take place, and in any case would be impossible; at the same time these insects possess ovaries (undeveloped). There is still another Japanese race available (of unknown origin), and if males of this race are crossed with Schneidemühl females a further stage is reached in this extraordinary series. The F_1 females are intersexuals of high grade, in fact externally they can scarcely be distinguished from males, although careful search reveals still a trace of the female features (see Fig. 46). The instincts are altogether male in character, and furthermore the organs of reproduction are affected to such an extent that all stages of the transformation of the gonads may be found, from examples with an ovary to those with testis and even ripe spermatozoa. Such a transition stage is illustrated in Fig. 47. Only one stage further is lacking, namely, a cross by which all the females will be converted into males, and this is supplied by crosses of two other Japanese races (Ogi and Aomori) with Schneidemühl, Fiume, or Hokkaido females. These alterations or conversions are not inferred but demonstrated embryologically[2] as well as by testing the gametic nature of the changed

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[1] The nomenclature of the races in the following section refers only to the locality from which our first material, of the condition described, came.

[2] Goldschmidt, R., and Saguchi, S., "Die Umwandlung des Eierstocks in einen Hoden beim intersexuellen Schwammspinne." Zeit. f. ges. Anatomie, 1922.

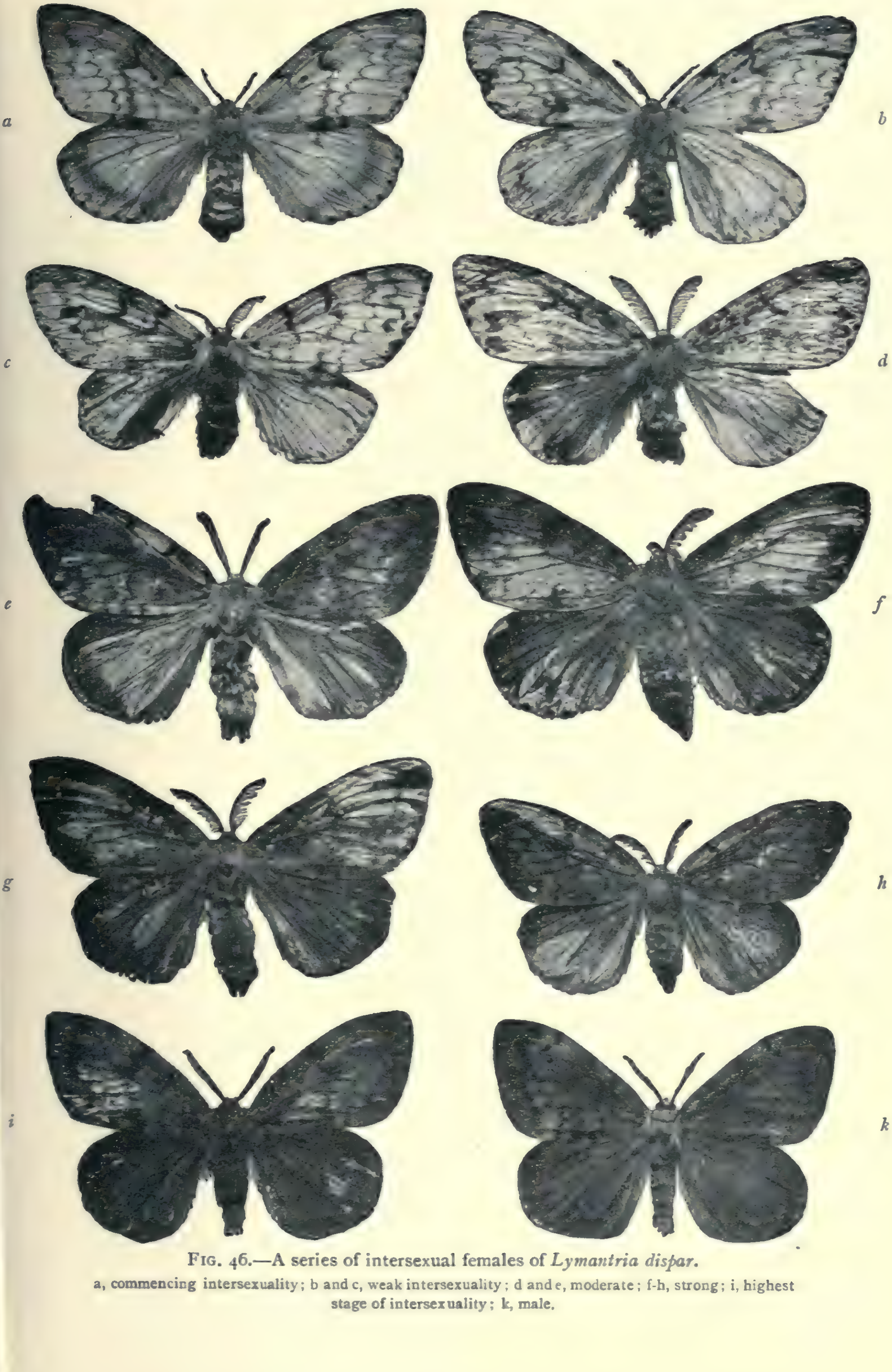

FIG. 46.—A series of intersexual females of *Lymantria dispar*.

a, commencing intersexuality; b and c, weak intersexuality; d and e, moderate; f-h, strong; i, highest stage of intersexuality; k, male.

animals.[1] The series of stages that we have described are illustrated in Fig. 46.

If we would discover the meaning of these results it is necessary in the first place to emphasize the fact that both the eggs and sperm cells of all the races employed in the crosses are quite normal in regard to sex inheritance. In the right combinations they give only normal sex results. Since, however, these very cells in hybrid combinations are responsible for the occurrence of intersexuality, it is obvious that for the production of the normal sex result they must stand in some particular kind of relationship to each other, some condition which is upset, or no longer occurs, in hybridization cases. What is this relationship or attunement? The following important facts point to a method of explanation. A series of intersexes result when one and the same race as father is crossed with different races of females. But if one and the same race as mother is crossed with a series of males of different races, a typically different result is obtained which can also be arranged in an intersexual series.

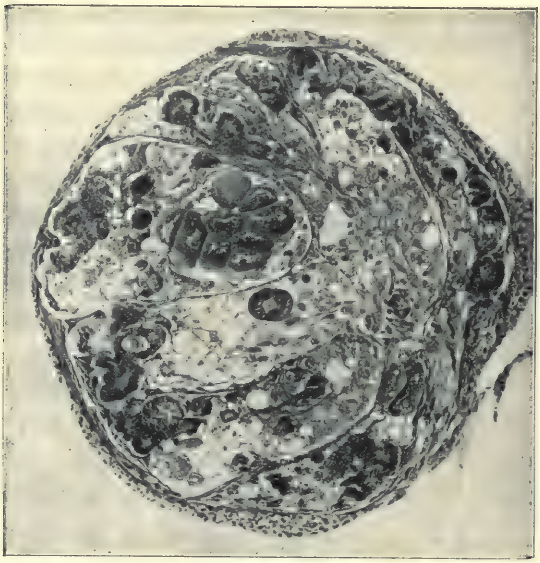

FIG. 47.—Section through the reproductive organ of a highest grade intersexual ♀ of *Lymantria dispar*, showing degenerating eggs and the transformation into testis tissue. The coarse structure is that of a testis.

This indicates that the result depends on a relationship of something situated in the eggs to something in the spermatozoa, a relationship which is different from the normal, in short, a disagreement. Now the degree of this disagreement changes in a similar manner with eggs of the one origin crossed with sperms of different origin as well as with sperms of one origin crossed with eggs of different origin. Therefore it must be concluded that a definite quantitative relation exists between the two sorts of sex-determining substance which is normal, and that any other quantitative relations produce intersexuality, the stage of which is proportional to the degree of divergence of such quantitative relation from the normal. Coming now to the concrete: What is really this disagreement and what are the determining substances which are concerned? The following further conclusions may be deduced from the facts: 1. Each sex possesses the fundaments (*anlage*) of both sexes, since both can become intersexual. 2. Which of the sexes will unfold itself is determined at and by fertilization. 3. The normal determination of sex is bound up, as we have seen, with the X-2X mechanism. But as this does not prevent the occurrence of intersexuality and the transformation of one sex into the other, it cannot be the mere presence of these chromosomes or the factors contained within them which counts, but rather their quantitative effect. 4. The F_1 result and the subsequent segregation shows (bearing in mind that in cases of female heterozygotism the X chromosome of the female comes from her father) that one of the deciding factors in the formation of the actual sex is inherited in the X chromosome and, in our example, with female heterozygotism. 5. The result of the reciprocal cross, as well as the other combinations required for a proper analysis (and the occurrence of male intersexuality which has not been detailed here), shows that other factors which are also concerned in this sex determination are purely maternal in inheritance. There are reasons for suggesting that they may be inherited in the cytoplasm of the egg, although there is also the possibility of inheritance in the Y chromosome. The Y chromosome will also be purely maternal in its inheritance by the daughter. If it is a case of inheritance in the Y chromosome, this must naturally have already unfolded its action in the unripe egg. That is to say, it must have exerted some influence and occasioned some particular plasma constitution. For after the maturation divisions the eggs which are male determined will no longer possess any Y chromosome. Recent experimental work makes it very probable that the Y chromosome *is* actually concerned. 6. The fact that the same female race gives different results with different male races shows that the factor present in the X chromosome is different quantitatively in each race. 7. The fact that males of the same race give different results with different races of females indicates that the sex factors inherited through the egg can also be quantitatively different.

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[1] Goldschmidt, R., "Untersuchungen über Intersexualität, III." In the press.

Now if these conclusions are combined in the lucid and symbolic manner employed for Mendelian inheritance, we arrive at the following: Each sex contains the factors for both sexes and either sex fundament may become active. Which actually does develop depends exclusively on the quantitative relationship of the two factors. Let F denote the factor for femaleness and M the factor for maleness, then the formulæ for the two sexes will be (F) Mm = female : (F) MM = male. (The brackets round the F are to indicate that it is purely maternal in inheritance.) The female is heterozygotic in the factor for maleness, which lies in the X chromosome, whilst the male is homozygotic. The female factor, purely maternal, is handed on equally to every egg, in the cytoplasm or in the Y chromosome. F and M act independently of each other with a quantitatively determined power which may be termed the valency. The factor with the higher valency determines the result. The quantities are, however, of such an order that an M is weaker than an F and consequently in the female sex, where both are present, the M produces no visible effect. Two M's are, however, stronger than one F and thus in the male (see formula above) the F is overpowered. To make this and the following quite clear, let us suppose that we can measure the valencies of the factors and we find that the female (F) has a strength of 80 units, whilst that of the male factor is equivalent to 60 units. Then if the female formula is (F) Mm the F will be 20 units stronger than M. In the male, with formula (F) MM, the double dose of M brings the value of this factor to 120 units, that is to say, stronger by 40 units than the female fundament. Two possibilities may arise here. Either the smallest excess of one fundament over the other suffices to overpower the latter, or a definite minimum is necessary in order that the fundament of one sex shall triumph over that of the other—an epistatic minimum. Let us assume that the latter is the case and that this minimum in our example is 20 units, then we shall have a female if $(F) - M = > 20$, and a male if $MM - (F) = > 20$. Expressed in another manner, if we denote the difference between the valencies of the two sex fundaments as e, then the limiting values of e for the two sexes are $+ 20$ and $- 20$. This can be stated graphically as in Fig. 48, in which the values for e are arranged along a straight line. Individuals to the right of + 20 are male, whilst to the left of − 20 they are female, and in between these points we have the intersexual forms. If these are heterozygotic for M they are intersexual females; if they are homozygotic for M they are intersexual males.

How does this valency assumption explain the actual breeding experiments detailed above? Let it be granted that we have two races both of which are normal in regard to the quantitative relationship of their sex factors, yet having different absolute values for the valencies concerned. For simplicity's sake we may speak of strong forms when the valency for M is relatively

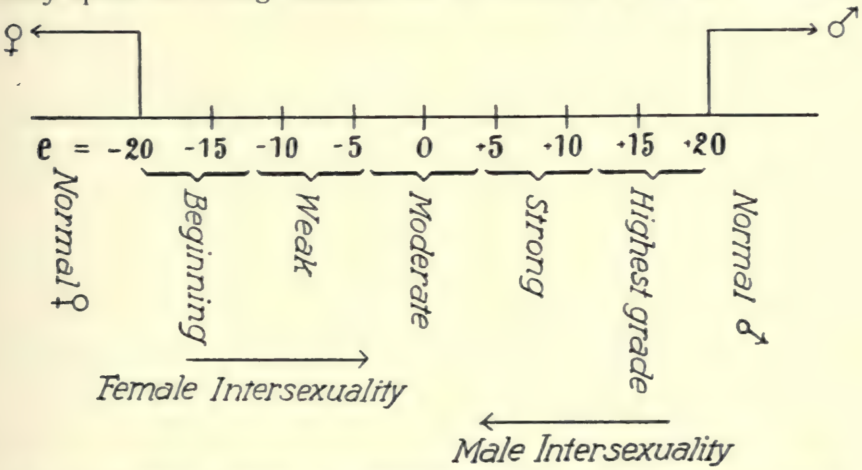
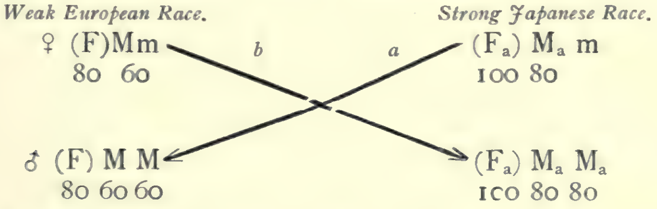

♀
♂
e = −20 −15 −10 −5 0 +5 +10 +15 +20
Normal ♀
Beginning
Weak
Moderate
Strong
Highest grade
Normal ♂
Female Intersexuality
Male Intersexuality

FIG. 48.—Diagram illustrating the intersexuality types as expressions of the valency differences F minus M.

high, and correspondingly of weak forms. We can then state the following as possible valency conditions:—


Weak European Race.
Strong Japanese Race.
♀ (F)Mm
80 60
b
a
(F_a) M_a m
100 80
♂ (F) M M
80 60 60
(F_a) M_a M_a
100 80 80

Both races will be sexually normal when pure bred. If, now, the Japanese female is crossed with a European male (arrow *a*), then in the F_1 generation we have—

F_1 ♀ (F_a) Mm and ♂ (F_a) M_a M
100 60 100 80 60

The value of e is + and − 40, and both sexes are again normal. The reciprocal cross to this is indicated by the arrow *b*, and it gives in F_1 :—

$$\begin{array}{llll} F_1 & \text{♀}(F)\ M_a\ m & \text{and} & \text{♂}(F)\ \ M_a\ M \\ & \quad\ \ 80\ \ 80 & & \quad\ \ 80\ \ \ 80\ 60 \end{array}$$

But now the female possesses no difference in the values of F and M, $e = 80 - 80 = 0$, and consequently these females are intersexual, exactly half-way between the sexes.

This scheme explains, without further details being necessary, the crosses described above. The actual series in the value of M in the races named is: *Weak races*, all European races, Japanese Hokkaido and South Japanese; *Strong races*, moderate Gifu, very strong Ogi, Aomori. For (F) the weakest race is Fiume, and then follow Schneidemühl and Hokkaido and lastly the southern Japanese races. Perhaps the clearest demonstration is the following :—

We have seen that the females of the weak race Fiume, when crossed with the moderately strong Gifu males, produce a rather high degree of intersexuality in the females of the F_1 generation. The same females, however, gave nothing but males when crossed with the very strong Aomori male. The Japanese females of the Kumamoto race give only weak female intersexuality in the F_1 generation when crossed with males of the Gifu race. Now according to this one would expect (if our theory is correct) that if these females (Kumamoto race) were crossed with Aomori males a middle degree of intersexuality would result, and such is actually the case. The diagram (Fig. 49), corresponding to Fig. 48, explains this without further details being necessary.

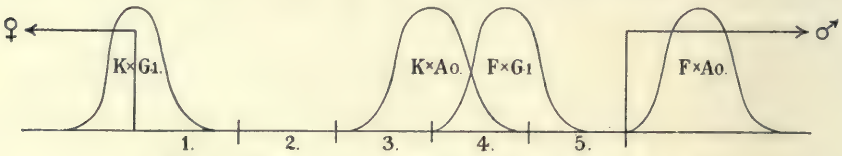


FIG. 49.—Intersexuality equation. Explanation in text.

We must now return to the intersexuality amongst the males. Fig. 50 illustrates a series of intersexual males resulting from the F_1 and F_2 generations of different crosses. It is not necessary to discuss this side of the case in the same detail, for it must be evident from what has already been said that any combination should produce intersexual males if in the formula of the male [(F)MM] a high valency F can be combined with a low valency M. The results fulfil the expectations.

Before we extend our analysis further, let us make quite clear how far this has carried us in regard to the nature of sex inheritance. We have again discovered the simple heredity mechanism of heterozygotism and homozygotism; but at the same time we have seen that the mere presence of the sex differentiators in homozygotic or heterozygotic condition is not sufficient to determine the sex. It appears rather as if

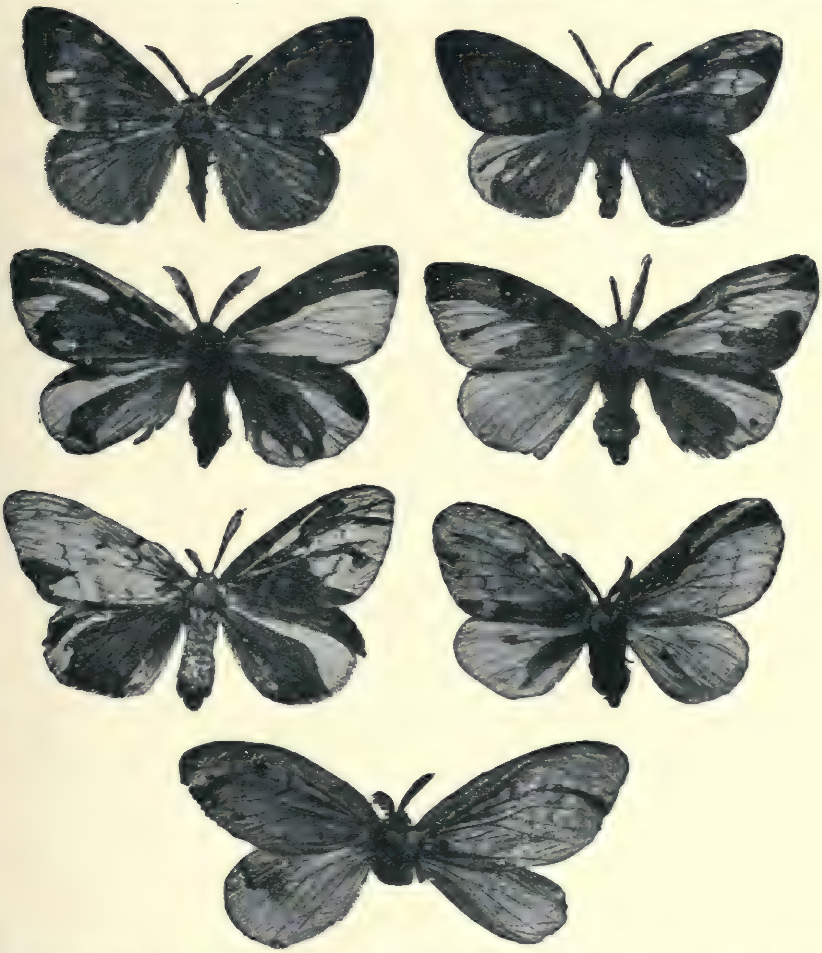


FIG. 50.—Series of intersexual males of *Lymantria dispar* L. from commencing intersexuality to strong intersexuality.

a definite degree of action of these sex factors were necessary so that those of one sex should overpower (or be suppressed by) the simultaneous and independent action of the other. The normal sex inheritance mechanism is responsible for the correct quantitative conditions, its mode of operation being to leave one complex constant (the maternally inherited (F)), whilst distributing the other in either the complete or the halved condition (M or MM, one X chromosome or two X chromosomes). But if the condition in regard to these quantities can be absolutely altered, the system remaining otherwise the same, no factor—or chromosome constitution—can prevent another and even contrary sexual condition manifesting itself. Thus we see that the sex inheritance mechanism of heterozygotism-homozygotism is a mechanism which is responsible for the distribution of sex-determining substances for both sexes in a definite quantitative relationship, so that one or the other substance group is in excess. But this means that we have progressed another stage on our way towards an understanding of the physiological meaning of the mechanism. In fact, the problem would be completely solved if we knew what the sex-determining substances were and how their quantitative effect was to be interpreted. A further analysis of zygotic intersexuality already supplies an answer to this question.

The concept of intersexuality might lead to the impression that an intersexual individual was one in which the character of *every* part of the body represented some definite intermediate stage between the two sexes. The details already given show, however, that such is not the case. On the contrary the various organs of the body differ in this respect; one may be normal whilst another is intersexual. Only purely quantitative characters, like the length of the antennal pinnæ, present intervening stages. Intersexuality is then to be regarded as a macroscopic phenomenon, a concept of the general habitus of an individual, which in reality is a kind of mosaic of differently sexed parts. Now it has been found that the various organs of the body fall into a definite series as regards their development of the intersexual character, and this series is exactly the opposite to the order of their embryonic differentiation. The organs which are first developed and differentiated, as for example the reproductive organs, are the last to be modified, whilst those which appear last (as for example colour of wings) are the first to be changed. The exact analysis of this has led to the discovery of what we may term the Time Law of Intersexuality. An intersex is an individual which has developed as a male (or female) up to a certain time point; from this turning point the development has continued as female (or male). The increasing degree of intersexuality is an expression of the recession of the turning point, that is, its occurrence at an earlier stage in development. And lastly, the condition of any particular organ is determined by the time of its differentiation—whether it is before or later than the turning point. This brings us to the following situation :—

1. Intersexuality occurs if, at a definite time point in development (the turning point), a reaction which we may term the "switch-over reaction" takes place. The physiological effect of this consists in forcing the alternative processes of differentiation to run in the direction of the other sex. Female differentiation changes over into male differentiation or the reverse takes place.

The morphological as well as the embryological investigation of the most diverse organs has given us this fact free from objection.

2. The time of the occurrence of the "switch-over reaction" is a measure of the degree of intersexuality; the earlier it lies the greater the degree of intersexuality.

3. The occurrence of the "switch-over reaction" during development is determined genetically through inheritable factors in the races crossed.

4. These heredity factors of sex differentiation differ amongst themselves in their valency = quantity.

5. Intersexuality is produced genetically when the factors for male and female differentiation are quantitatively incorrectly in tune or harmony with one another.

6. The extent of intersexuality is exactly proportional to the amount of this dissonance.

From this it follows :—

(*a*) Normal sex is determined when the *whole* series of differentiations takes place under the specific physiological influence which is called forth by the factor or factors of the particular sex concerned.

(*b*) Since in normal individuals either the male or the female differentiating influence is predominant, whilst in cases of intersexuality both influences can act one after the other in the same individual, the normal sex heredity mechanism must be such as gives one influence the upper hand.

(*c*) Since intersexuality is determined by the occurrence of the "switch-over reaction" during the development, and this event is induced through abnormal quantitative relations of the factor combinations, the predominating reaction controlling the actual sex in normal cases must be more rapid than that controlling the non-appearing sex.

Female intersexuality is occasioned when, notwithstanding the predominating female reaction, the male reaction runs more rapidly than normal and sooner or later overtakes it (the converse is the case for male intersexuality), and the more rapid the reaction, the earlier the turning point and the greater the intersexuality.

(*d*) We have thus co-ordinated the concept of quantity of heredity factors with velocity of reaction.

Now what is the nature of the reaction which influences differentiation? We can at this point give no answer to the question, but we may anticipate the discussions to a slight extent. The only known physiological activity which suits the case is that of the hormones. And hormones secreted by the reproductive organs are actually able, as the following chapter will show, to alter the nature of sex differentiation, whilst hormones from the thyroid gland can induce frog tadpoles to metamorphose irrespective of age. We conclude, therefore, that the reaction which is conditioned by the sex factors and occurs with definite velocity is the production of hormones of sexual differentiation.

In the female the production of female hormones is more rapid than that of male hormones, the opposite is the case in the male. The hormones which are present in greatest quantity have most influence over the differentiation.

Under ordinary circumstances the hormones of the opposite (non-appearing) sex are produced so slowly that an effective quantity is not present until development has come to an end. If, however, this production were speeded up through the presence of a greater quantity of heredity factor, the time point at which these hormones attained the upper hand would fall within the period of development and that would be the turning point.

The switch-over reaction in an example of intersexuality marks, therefore, the beginning of the domination of the hormones of the opposite sex.

If the sex factors, whatever they may be, go together with a reaction (viz. the production of hormones of sex differentiation), and if this reaction runs with a velocity which is proportional to the absolute quantity of these factors, it suggests that the heredity factors are things which follow the laws of mass action. But one is compelled to assume that the substance factors carried by the chromosomes are of extraordinarily minute volume, a volume which bears no relation to the size of the effect they produce. So one is naturally led to the conclusion that they are enzymes or substances of a similar chemical nature, substances which accelerate some specific reaction in proportion to the quantity present. The provisional solution of the problem of zygotic intersexuality may then be put as follows: Each fertilized egg possesses normally the two kinds of hereditary factors whose activity is necessary for the differentiation of the one or other sex. These sex factors are enzymes or bodies of similar physico-chemical nature. Each of these enzymes (that of male as well as of female differentiation) is necessary for the performance (acceleration) of a reaction, the products of which are the hormones of sex differentiation. In species with female heterozygotism like the Gipsy moth, the female enzyme (to put it this way for brevity) is purely maternal in inheritance, so that every egg is identical in regard to the factor for femaleness. The male enzyme is the sex factor carried by the X chromosome, and in accordance with the well-known heterozygote-homozygote scheme it will be present in this example in half the eggs and in all the spermatozoa. The absolute quantity as well as the relative quantity of the two enzymes is a fixed hereditable character of a race.

The mechanism of sex inheritance (which consists in the distribution of two X chromosomes, two factors M, or two doses of male enzyme, to the eggs that will become male individuals, but only one X chromosome, etc., to an egg destined to produce a female) is accordingly a mechanism which decides whether at the commencement of development n or two n-units of male enzyme will be opposed to a definite (and always equal) quantity q of female enzyme. These quantities are so graded that the quantity q of the female enzyme is greater than n of the male enzyme, and so the production of hormones of female differentiation are speeded up in this combination and the development is female. On the other hand, two *n* of male enzyme is a higher concentration than *q* of the female, thus the hormones of male differentiation will be produced more rapidly and a male will be developed by this combination. The X chromosome (heterozygote-homozygote) mechanism serves in this way as an ideal device for balancing the relations of two velocities of reaction.

Since it is the *relation* between two quantities which is the deciding factor, the absolute quantities can be very different so long as the proper relation is upheld and the resulting velocities of reaction are in harmony with the time conditions of development. As a matter of fact, different races do vary, as we have seen, in regard to the absolute quantity of the enzymes, and if two such races are crossed the proper quantitative relation can be destroyed, and the male enzyme even in the one *n* quantity may be too strong for the female quantity. The contrary may also take place, and the female enzyme be too concentrated even for the two *n* quantity of male enzyme. We have followed the consequences of this; the products of the abnormally concentrated enzyme are formed too rapidly, an effective amount is accumulated during the period of development and intersexuality results.

In the course of the formal Mendelian analysis of the phenomenon given above it became evident that the assumption of a simple excess of valency of the male factors over the female (or the converse) was insufficient for the complete explanation of the case. It would explain change of sex but not the different grades of intersexuality. We introduced therefore the conception of an epistatic minimum, the assumption that a definite minimal surplus of one quantity over the other was necessary in order to decide the sex. In other words, the high concentration of one of the two enzymes is not alone decisive for the production of pure sexes—a minimum of difference between the two is necessary. Then between the two minima, namely, that for M—F and that for F—M, there lies a series of difference values which induce intersexuality. The condition can be represented by a series of curves marking the production of male or female hormones. In normal cases the form of the two curves will be such that they do not intersect during the period of differentiation of the organism. However, by the introduction of a variable

—the initial concentration, the same kind of curves must intersect during development, the point of intersection being proportional (or inversely proportional) to the value of the variable. The curves of hormone production in the different intersexuality experiments (female intersex) might thus run as in Fig. 51, where the time of development is taken as constant—which is not really the case. (The correction, consisting of a transposition of the line S—S, which indicates the end of differentiation, to the right or left, can easily be applied.)

F is the curve of production of the female hormones, Mm the curve of the male hormones in a normal case (for the female),

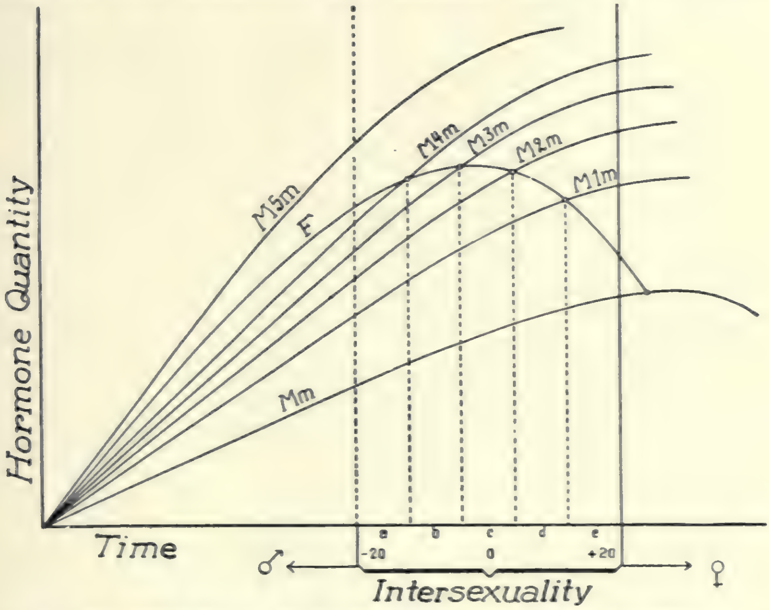


FIG. 51.—Graph illustrating the physiological interpretation of intersexuality. Explanation in text.

M_1m, M_2m, etc., are the curves of male hormone production in different grades of female intersexuality. The points of intersection of the F and M curves indicate the "turning points" in the different examples. A vertical line dropped from each to the abscissæ gives the scheme used previously (see Figs. 48 and 49) for intersexuality.

Previously there was no other case known which permitted of such a detailed analysis[1] as that of the Gipsy moth, but the phenomenon is undoubtedly more widely distributed. As a matter of fact the number of communications on cases of intersexuality increases every day. In most of them, however, it is very difficult to decide whether the phenomenon is the same as that present in the Gipsy moth or not. It is necessary in the first place to keep the term and the conception intersexuality for the phenomenon where an animal develops up to a particular moment, the turning point, with the character of one sex, then a change occurs and the individual continues and completes its development with the character of the other sex. In all the recently discovered cases of zygotic intersexuality, the embryological analysis is wanting. Perhaps, however, it is legitimate to speak of intersexuality even when the above definition does not apply, for it is conceivable that with the same genetic cause (quantitative condition of the sex factors) different consequences from the point of view of the physiology of development might result. When it is a matter of species crosses, the manner of the reciprocal action of F and M towards the other determining factors of development might be such as to give an apparently altogether irregular result. There is no point in going into details here since the embryological material is lacking.

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[1] Partial results agreeing with ours in the essential features have been obtained by Brake, Standfuss, und Schweitzer; see Goldschmidt und Poppelbaum, 1912, 1914.

Such types of intersexuality which are not altogether clear have become known as the result of species crosses amongst butterflies, *Drosophila* and crustacea, without any knowledge of the cause of their appearance being available; also in *Drosophila* as the consequence of abnormal chromosome constitution. Harrison[1] has obtained results which belong to this category in his species crosses of *Biston.* In his experiments, males of the Hirtaria type (see Fig. 52) crossed with females of the Græcaria-, Alpina-, and Zonaris-groups give exclusively male offspring.

The cross Zonaria-females × Rachelæ-males gives males and intersexual females, whilst the reciprocal cross is normal. Details of these and other crosses agree very well with the interpretation worked out above, and as a matter of fact Harrison accepts our quantitative theory. In spite of this the case does not yet appear absolutely clear, for a recent anatomical investigation carried out by Meisenheimer[1] showed that the reproductive organs of these intersexes had quite a different anatomical nature from those of *Lymantria*, and a still unexplained complication evidently underlies the whole. Again, intersexes which Sturtevant[2] obtained as the result of species crossing with *Drosophila* still await an explanation.

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[1] Harrison, J. W. H., and Doncaster, L., "On Hybrids between Moths of the Geometrid Sub-family Bistoninæ," etc. Journ. Genetics, 3, 1914.—Harrison, J. W. H., *ibid.*, 1916.

We are just as far from obtaining a correct idea of intersexuality in the Crustacea. Kuttner described some time ago a Daphnid stock found in nature which produced intersexes regularly in each generation. Banta[3] has since then rediscovered

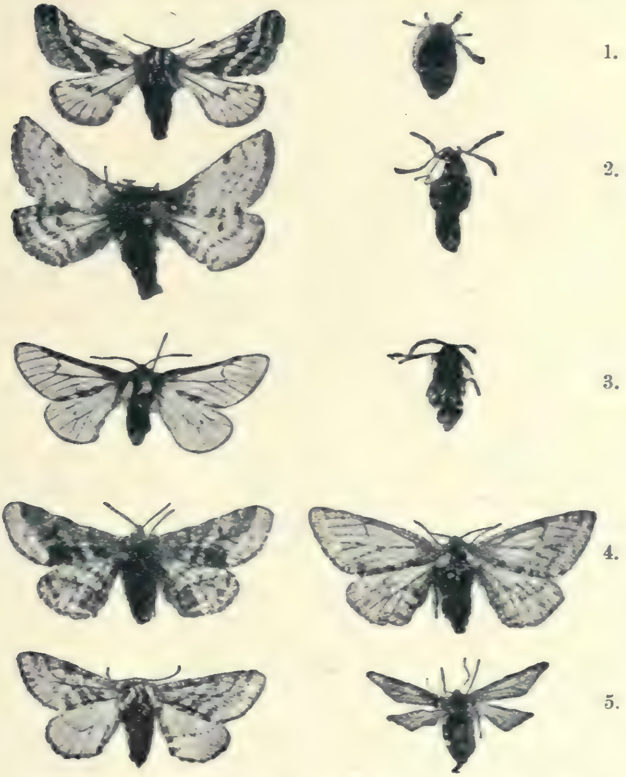

FIG. 52.—Bistonidæ, males on the left, females to the right.

1, *Nyssia zonaria*; 2, *N. græcaria*; 3, *Pœcilopsis radelæ*; 4, *Lycia hirtaria*; 5, *Pomonaria* ♂ × *hirtaria* ♀.

After J. W. H. Harrison.

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[1] Meisenheimer, J., "Verh. deutsch. zool. Ges." Würzburg, 1922.

[2] Sturtevant, A. H., "Genetic Studies on Drosophila simulan." Genetics, 5/6, 1920-21.

[3] Banta, A. M., "Sex Intergrades in a Species of Crustacea." Proc. Nat. Ac. Sc. Washington, 1916.

such a line and followed it through numerous generations without obtaining any clear explanation of its origin or its developmental physiology. More recently still de la Vaulx[1] has procured a similar stock and has investigated in detail the series of intersexuals of all stages which he obtained from it. He is inclined to accept our explanation, but he could not produce the intersexes experimentally and therefore explain their origin.

The same thing applies in regard to the intersexual *Gammarus chevreuxi* studied by Sexton and Huxley.[2] These authors believed they had a real case of intersexuality similar to that of the Gipsy moth, but nothing is known of the causes leading to its origin.

The position is better in regard to the triploid intersexes of *Drosophila* described by Bridges.[3] Here the cause of the intersexuality at least is known, that is, the presence of abnormal numbers of chromosomes. Bridges was able to breed *Drosophila* which were triploid, that is, they possessed three sets of chromosomes instead of two ($3n = 12$ instead of $2n = 8$). Amongst the progeny of these triploids there occurred intersexes, and it was found that they possessed three sets of autosomes but only two X chromosomes. Here also the intersexes presented all stages between maleness and femaleness, but up to date no embryological analysis has been forthcoming which would permit of making comparisons with the *Lymantria* intersexes.

It is well worthy of note that Bridges finds himself compelled, as the result of his observations, to draw in principle the same conclusions concerning the physiology of sex determination as we have drawn from our *Lymantria* experiments. He also concludes that the sex is determined through a quantitative relation between determination factors within the X chromosome and such without. The latter were in the autosomes whilst in *Lymantria* they were at least in part in the Y chromosome. The female determiner lies in the X chromosome (naturally the converse from *Lymantria* since in *Drosophila* it is the male sex which is heterogametic whilst in *Lymantria* it is the female);

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[1] Vaulx, R. de la, "L'intersexualité chez un crustacé cladocère *Daphnia Atkinsoni* Baird." Bull. biol. France, Belg., 55, 1921.

[2] Sexton, E. W., and Huxley, J. S., "Intersexes in *Gammarus chevreuxi* and Related Forms." Journ. Mar. Biol. Ass., 12, 1921.

[3] Bridges, C. B., "The Origin of Variation in Sexual and Sex-limited Characters." Amer. Nat., 56, 1922.

the male determiner is in the autosomes. False quantitative relations between the two are supposed to call forth intersexuality. Thus Bridges also falls in with our view in all the decisive points, with the single difference that instead of speaking of the different quantities of a sex factor he prefers to speak of a more or less greater number of part factors. Logically as well as physiologically this is naturally the same. It should not be forgotten, in passing, that it was Standfuss[1] who first drew attention to the probability of the existence of triploid intersexes and attempted to explain them with the help of our *Lymantria* work.

Thus the study of zygotic intersexuality has shown us how the substances which are distributed by the mechanism of sex inheritance act in determining sex. But there is a point where the analysis must stop. What sort of a reaction is it whose influence is so decisive in regard to sex? We have already stated in answer to this question, that it must be the production of hormones which control sexual differentiation. This conclusion, however, can only be established after we have made a study of hormonic intersexuality, and this will be the aim of the next sections.

3. Hormonic Intersexuality

We speak of hormonic intersexuality when sex-intergrades are not the result of the properties of the gametes which meet at fertilization, but are produced later by specific chemical influences (now grouped under the head of hormone action). In regard to the chemical nature of these hormones little can be said; it would appear as if all sorts of substances can act as hormones. They are characterized more by their action, their influence on growth and processes of differentiation, as also on physiological functions. They are not all produced in the organism in the same way, and from the point of view of our special problem two types come under consideration, external secretions and the so-called internal secretions. The latter phenomenon is the one which receives most notice when the question of hormones is under discussion. Under this head one puts a chemical action of certain special organs, the thyroid gland, the thymus, the adrenal body, hypophysis, pancreas and reproductive organs of the Vertebrates, an action which has a marked influence on growth, differentiation, and function. The classic examples are the influence of the hormones of the pancreas on metabolism and the hormones of the thyroid gland on growth.

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[1] Standfuss, Mitt. Schweiz. Entom. Ges., 12, 1914.

Now in those organisms where internal secretions localized in particular glands are necessary for the normal growth and functions (and this is particularly the case for Vertebrates), one also finds that the special processes of differentiation which occasion the differences between the sexes are more or less dependent on an internal secretion originating in the gonads. It follows from this fact that only the relation of hormones to the external attributes of sex, i.e. the secondary sex characters, is likely to come under our notice in the first place. The sex glands themselves, and therefore the sex, must of course be already present before any specific influence of these glands is exerted. Only under special circumstances can it be possible to study the relations of hormonic action to the total sexuality, an investigation which must naturally be of the greatest importance. Let us first consider, therefore, the importance of the hormones of the already differentiated sex glands for the secondary sexual characters.

a. Internal Secretions and Secondary Sexual Characters

In considering the facts to be detailed under this heading one point must be clearly kept in mind—the internal secretion of the reproductive organs, like that of the other organs mentioned, is no simple phenomenon. It is associated in the most diverse manner with processes of growth and functions of the body, and stands, moreover, in close relationship to the function of other glands of internal secretion (ductless glands).[1] Consequently when we study the effects of castration or transplantation of the gonads we must separate the resulting general physiological condition from that which is really of importance to the sex problem. This has not always been done and many errors have crept in as a result. Similarly it has not been sufficiently realized that different species of organisms vary in their ability to make considerable morphogenetic alterations in their adult stages.

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[1] Tandler, J., und Grosz, S., "Die biologischen Grundlagen der sekundären Geschlechtscharaktere." Berlin, 1913.—Harms, W., "Experimentelle Untersuchungen über die innere Sekretion der Keimdrüsen." Jena, 1914.—Biedl, A., "Innere Sekretion," 2 Aufl., 1913.

Conclusions must be based, therefore, on positive rather than on negative results. Where many authors have come to the conclusion that castration only brings about an asexual or juvenile alteration to the secondary sexual characters, in other words, causes the body to return to the general character of the species free from the alterations produced by sex, they have also based their studies on cases which for specific reasons have not given a clear result. For example, if the idea is correct that the alteration of the larynx in eunuchs is a mere cessation of development and not a step in the direction of female development, the experiment is of great significance from the point of view of the relationship between growth and internal secretion, but of no primary importance for the sex problem. We consider it justifiable therefore to draw conclusions only from positive results.

Now there are two lines of experiment which above all have given harmonious and definite results, namely, the castration and transplantation experiments on mammals and birds. Both are based on a series of long-known facts, facts which led Berthold long ago to the statement of the theory of the internal secretion of the reproductive organs. They comprise observations on the alteration of secondary sexual characters resulting from castration carried out for economic purposes, or from involution of the gonads in consequence of age or some pathological condition, and perhaps the most striking example is the cock feathering of old hens, hen-turkeys, etc.

The chief points arising from the systematic study of the phenomena are given below.

The first definite series of investigations were the extraordinarily important experiments carried out on rodents by Steinach.[1] But for their proper understanding a word or two is necessary on the seat of the internal secretion of the reproductive organs. Up to date there are two opposing views in regard to this matter, and the accuracy of the one or other is still undecided. According to that of Ancel and Bouin the internal secretion of the gonads is the product of the so-called interstitial tissue (also termed the cells of Leydig). It has been found possible to destroy the actual germinal tissues (spermatozoan tissue) by Röntgen rays, or by transplantation, without the destruction of the interstitial tissue, but when this has been done the normal hormone action continues to take place. It would appear, therefore, to be the interstitial tissues within the gonad which are responsible for the specific internal secretion effect (Fig. 53). This view is upheld by Steinach, Lillie, Lipschütz, and others (to mention a few of the chief supporters). The other opinion is that put forward in particular by Stieve and Harms.[1] According to this view the seat of the hormone production lies in the sex cells and their derivatives. From the point of view of our observations it is all the

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[1] Steinach, E., "Willkürliche Umwandlung von Saugetiermännchen," usw. Pflüger's Archiv., 144, 1912.—"Feminierung von Männchen und Maskulierung von Weibchen." Centrbl. Physiol., 27, 1913.

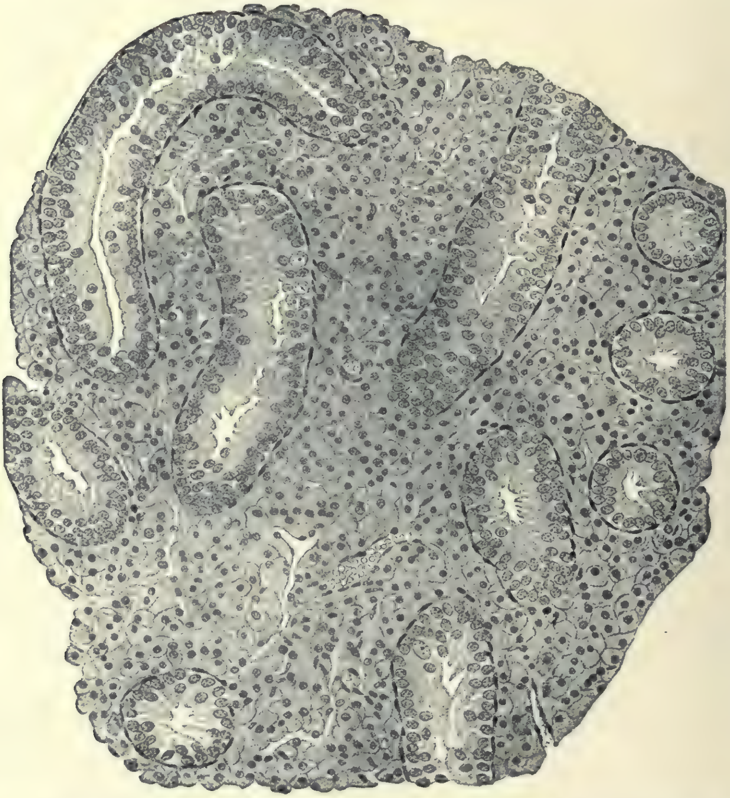

FIG. 53.—Section through a mammalian testis with sperm ducts and interstitial gland tissue. After Tandler-Grosz.

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[1] Ancel, P., et Bouin, P., "Recherches sur la structure et la signification de la glande interstitielle," etc. Arch. Zool. exp. S. 4, V, 2, 1904. Extensive references to the literature (from both points of view) are given by Stieve H., "Entwicklung, Bau und Bedeutung der Keimdrusenzwischenzellen." Erg. anat. Entwicklungsgesch., 23, 1921.—Lipschütz, J. A., "Die Pubertätsdruse und ihre Wirkungen." Bern, 1919.

same which of the above is correct, the feature of real importance is the fact that the gonads as a whole are the seat of a hormone production.

Castration in the Mammalia results in a cessation of the normal development of the secondary sexual characters. The specific hormones are necessary, therefore, for their complete development. Their absence, however, does not bring about the development of the secondary sex characters of the opposite sex. Now Steinach castrated young rats and guinea-pigs and then transplanted ovaries into them. When healing had taken

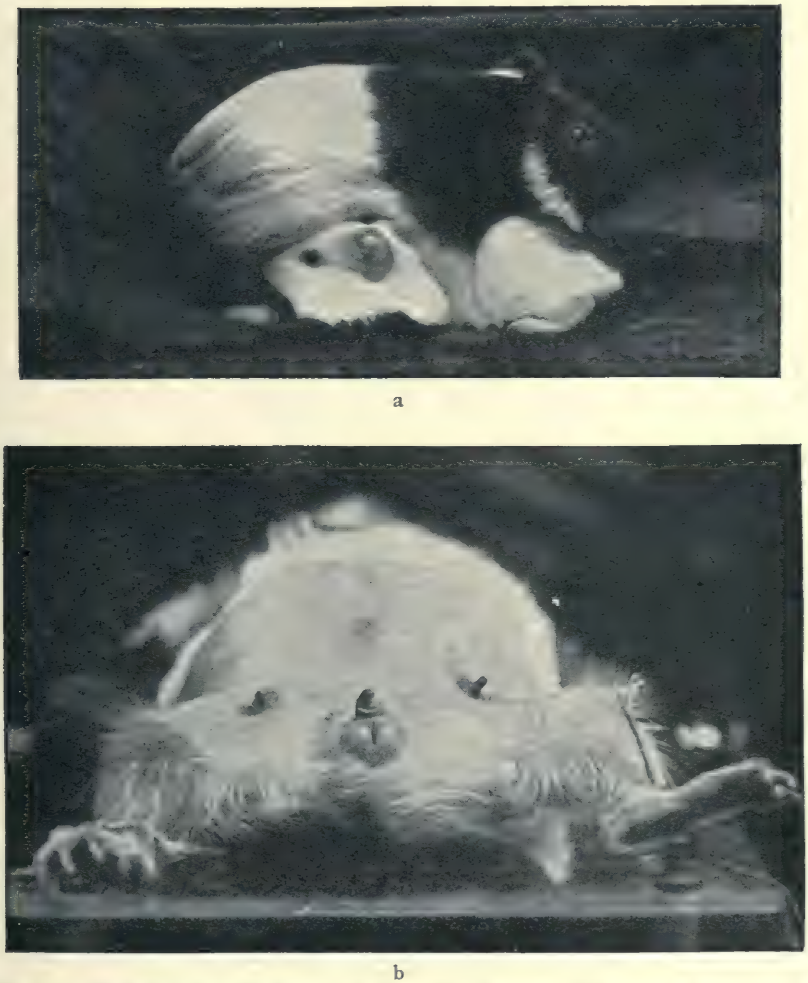

FIG. 54.—Feminized male guinea-pig; upper figure suckling, lower figure demonstrating the teats. After Steinach.

place and function was restored the gonad commenced to exert its specific influence. Male organs which had already been differentiated ceased to develop further or retrograded, whilst organs which could continue their growth in modified form developed in the female direction and in the end became altogether female in character. The final result was that such feminized males became exactly like females in form, weight, skeleton, and character of the hair. Their mammary glands and teats developed as in a female and even secreted milk; at times the instinct of suckling was present (Fig. 54). Sexually these modified males behaved exactly like females towards the normal males, and their effect upon the latter was the same as that of ordinary females.

The opposite experiment to the above was also successfully carried out by Steinach, and castrated females with introduced testes took on the male development. In form, external appearance, and sexual instincts they resembled males and the vaginal opening partly or completely disappeared.

This investigation (which has since been considerably extended in various details, and supported so far as the features of general theoretical importance are concerned, if not in all the details)[1] presents the following points for our problem: *The complete development of the secondary sexual characters of the Mammalia is dependent on the presence of specific hormones. The presence of the hormones of the opposite sex causes the further development to follow in the direction of that sex and, so far as is morphogenetically possible, makes the individual intersexual.*

The results obtained with birds agree in principle with those obtained from the mammalian investigations. The chief difference is that with birds, at least in the female sex, mere castration alone is often sufficient to cause the appearance of the characters of the opposite sex. This is particularly striking in the case of ducks, as is illustrated in Fig. 55. The most successful experiments in this direction were carried out by Goodale, and on hens as well as ducks.[2] Leaving out details one may say that in the female sex castration results in the appearance of male characters, the extent of this development varying so that

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[1] Steinach, W., "Pubertätsdrüse und Zwitterbildung." Arch. Entwicklungsmechanik, 42, 1916.—Lipschütz, A., "Prinzipielles zur Lehre von der Pubertätsdrüse" (further citations are to be found here).—*Ibid.* 44, 1918.—Sand, K., "Experimentelle Studies over Konskarakter hos Pattedyr." Kopenhagen, 1918.—Moore, C. R., "On the Physiological Properties of the Gonads as Controllers of Somatic and Psychical Characteristics, IV." Journ. Exper. Zool., 33, 1921.

[2] Goodale, H. D., "Gonadectomy." Carneg. Inst. Pub., Nr. 243, 1916.

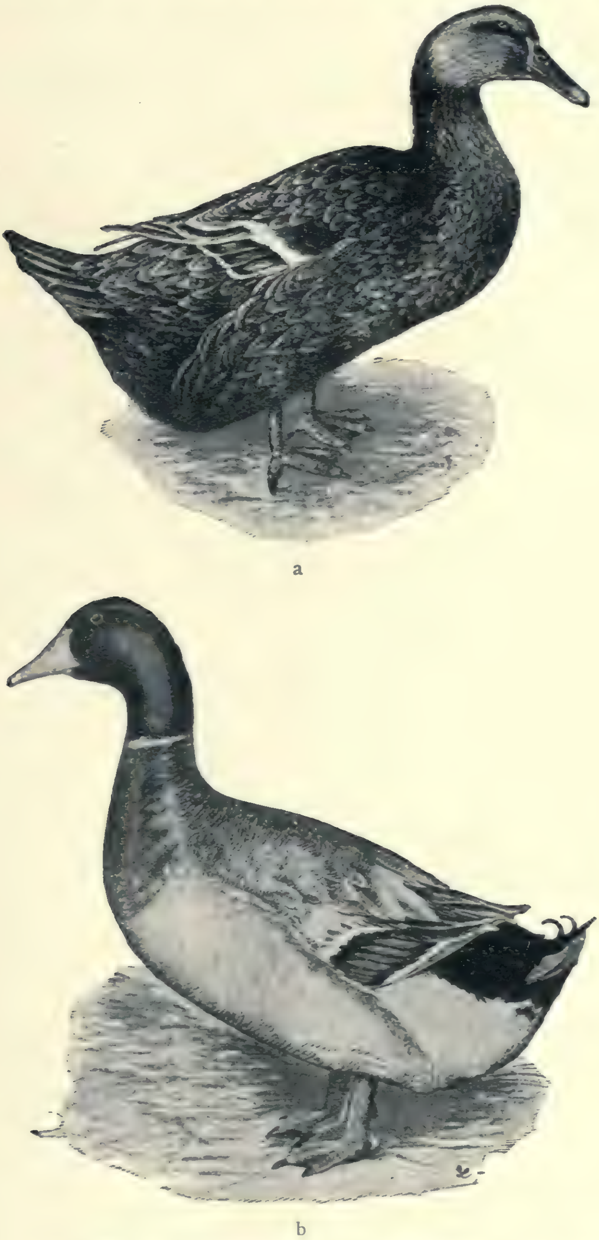

Fig. 55.—a, Rouen duck; b, Rouen drake. After Goodale.

something of a series of intersexual forms is obtained. With the male sex, however, feminization only occurs after the transplanting of ovaries into the castrated males, the conditions being analogous to those of the Mammalia.

Unfortunately the problem of the relations between internal secretions of the gonad and sex development is not so simple as would appear from the results described above. The difficulties come from different sides. On the one hand there is the case of the Amphibia. Almost every investigation carried out up to date has led to different results.[1] To illustrate this we might mention the fact that according to Meisenheimer transplanted ovaries, as well as testes, call forth the development of the thumb pads in frogs. It is clear that the gonad hormones do not work quite as simply as we have demonstrated in the previous pages. And as a matter of fact the same thing is indicated when we look a little further into some of the bird experiments. Old hen birds with degenerated ovaries develop male plumage—

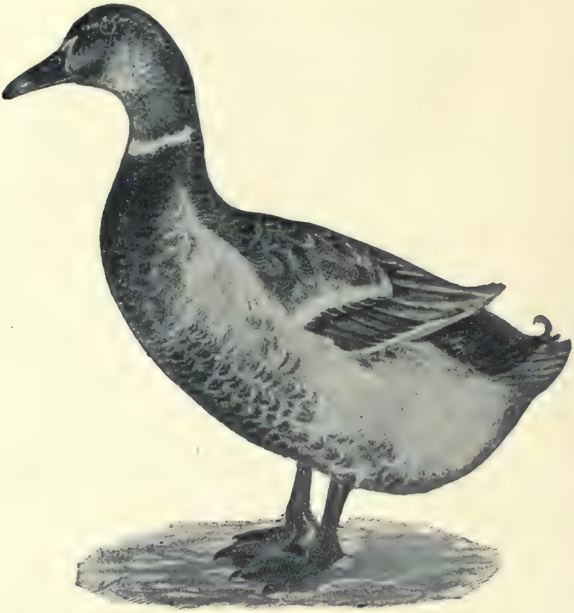

FIG. 55C.—Castrated Rouen duck. After Goodale.

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[1] Meisenheimer, J., "Experimentelle Studien zur Soma und Geschlechtsdifferenzierung, II." Jena, 1912.—Nussbaum, J., "Hoden und Brunstorgane des braunen Landfrosches." Pflüger's Arch., 126, 1909.—Smith, G., "Studies in the Experimental Analysis of Sex, V, VI." Qu. J. Micr. Sc., 56, 57, 1911.—Harms, W., "Hoden und Ovarialinjektionen bei Rana fusca-Castraten." Pflüger's Arch., 133, 1919.

there are even statements to the effect that testis or male gonad tissues develop. The same cock feathering develops after castration of females (ducks). Consequently the hormones of the ovary must exert some repressing influence on the characters of the opposite sex. The fact that the latter develop at all after the elimination of the reproductive organs shows, however, that in the birds there is something of the insect type—the centralized hormone production is not absolutely necessary for sexual differentiation. The same thing exactly is illustrated by another important fact, the presence of gynandromorphism in birds. We shall see later that gynandromorphs are sex mosaics occasioned through the abnormal distribution of the sex chromosomes. The cellular constitution of the different parts of the body decides the sex of those parts. Now if the hormones of the gonads were the deciding factors, it would be impossible to have such gynandromorphs in birds, since obviously the same hormones circulate through the whole body.

This does not exhaust the difficulties by any means, and another case that may be mentioned in this connection is Morgan and Punnett's series of experiments with the Sebright bantam cocks. In this race the cocks have a female type of plumage. If they are castrated they develop a rich male plumage (Fig. 56). *Thus the hormones of the testis in this case actually suppress the development of male plumage on a male bird.* Crosses between these cocks and normally feathered races show, however, that the specific hormone production is dependent upon the presence of a Mendelian factor.[1]

It must be granted that at the moment the difficulties which these facts oppose to a simple solution cannot be explained away, and many more experiments will yet be necessary. It appears to us[2]—and this must be accepted as simply a preliminary statement—that in birds (and probably also Amphibia) two quite different phenomena are taking place at the same time, and up to the present it has not been possible to disentangle them. There is an internal secretion localized in the gonad which influences the rhythmical appearance of rutting organs, breeding plumage, etc (Steinach's puberty gland). So much at least follows from the contradictory experiments on Amphibia; it shows itself again in Goodale's discoveries that the castrated drake does not produce the summer plumage (which is like that of the female in character), and that castration has a disturbing influence on the whole process of moulting. All this (as Goodale himself stresses) has nothing to do with the problem of sex determination, but belongs rather to the class of hereditable rhythms within the sphere of sex, as, for example, Œstrus, etc. The other phenomenon which overlaps this is the significance of the sex gland hormones for sexual differentiation itself.

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[1] Morgan, Th. H., "The Nature of the Gene." Amer. Nat., 1917.—Boring, A. M., and Pearl, R., "Sex Studies, IX." Anat. Record, 13, 1917.—Morgan, Th. H., "The Effects of Castration of Hen-feathered Campines." Biol. Bull., 39, 1922.—Punnett, R. C., and Bailey, P. G., "Genetic Studies in Poultry, III." Journ. of Genetics, II, 1921.

[2] Goldschmidt, R., "Intersexuality and the Endocrine Aspect of Sex." Endocrinology, 2, 1918.

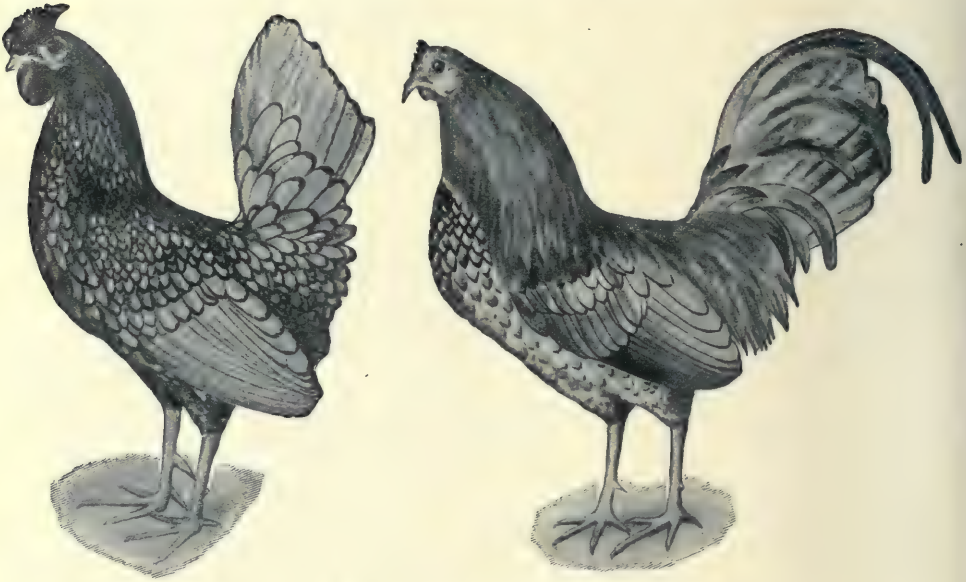

FIG. 56.—Sebright bantam cocks.

Left, normal hen-feathered male; right, the same bird with male plumage as result of castration.

The position may then be stated as follows: In birds the genetic situation is like that found in the Insecta. Every cell possesses from the time of fertilization both the sex enzymes and these, in proportion to their quantity, speed up in each cell the production of the hormones of sexual differentiation. Add to this, however, an important difference. The insect terminates its development with a single short sexual existence and then dies, whilst the bird slowly reaches sexual maturity and retains it for years. Now if everything were the same in insects and birds, so far as sex determination was concerned, the birds would change their sex, that is, become intersexual, in the course of their life. And this would take place from the moment where the curve of the other and slower sex reaction intersects with that of the more rapid reaction (see Fig. 51). This change, however, is prevented through the production of inhibiting hormones by the sex glands.[1] As soon as such production ceases (as in old birds) intersexuality begins and proceeds so far as the physiology of the processes of differentiation permits. Possibly in the Mammalia the last stage in the centralization of the control of sex differentiation has been reached, and the production of hormones of sex differentiation has been transferred from the individual cells to the interstitial cells of the gonads. If that were the case, gynandromorphism would be impossible in this group. As indicated above, we regard all these points as not yet ripe for discussion, and for this reason have refrained from going further into details.[2] Our main purpose will be served by reference to an important example of real hormonic intersexuality which is described in the next section.

b. Real Hormonic Intersexuality

Up to the present time only one case is known which can be safely classed in this category. This is the remarkable "hermaphroditism" of one partner in many cattle twins. Twin births from cattle are as a matter of fact not common. Now from the point of view of sexuality four types may occur, namely: (1) two males, (2) two females, (3) a male and a female, (4) a normal male and a sexually abnormal calf. When the twins are of unlike sex the fourth type is actually the rule and the third the exception. The sexually abnormal individual (termed the freemartin in English—the *Zwicke* of the Austrian Alps) is usually female in its external sex characters and more male internally. A very satisfactory explanation of this striking case has been supplied first by Keller and Tandler, and later by the same authors and by F. Lillie,[1] who worked out the case without knowledge of the further work of these authors. The investigation has increased the importance of the example from the point of view of our problem.

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[1] Steinach has brought forward evidence that in mammals the gonad hormones (puberty gland) inhibit the development of the characters of the other sex just as they advance their own.

[2] The position as regards the mammalia is discussed in detail by Steinach and Lipschütz (Arch. Entwicklungsmech., 42, 44).

It had first to be decided whether the freemartin was genetically male or female. All the earlier investigators[2] were of opinion that it was male, and moreover a partner of twins arising from one egg (Spiegelberg, Hart, Bateson, Cole). (Twins of this type arise through the abnormal and complete fission of a fertilized egg into two parts, each of which develops into a complete and perfect individual. They are always of the same sex.) Lillie, has, however, demonstrated in two ways that this is not the case. If the normal sex ratio is 1 : 1, then when twins are produced and each individual is the product of a separate egg, the laws of probability would lead one to expect the three possible sex combinations in the proportion 1 ♂♂ : 2 ♀♂ : 1 ♀♀. This is actually the case with lamb twins, as is indicated by an actual set of statistics giving 38 ♂♂ : 67 ♀♂ : 34 ♀♀. Where twins from a single egg are frequent (as is the case in man) the result is somewhat different. Lillie cites figures from Nicols giving 234497 ♂♂ : 264089 ♂♀ : 219312 ♀♀. If the cattle twins are stated numerically in a similar manner, the result indicates that a twin pair including a freemartin must be regarded as ♂♀. It also indicates that these twins are two egg twins and that the freemartin is genetically a female. The former is proved without any doubt by the fact that in all investigated cases of this kind the ovaries had two *corpora lutea*, as Tandler and Keller first discovered, whilst in all normal cases of the birth of a calf only one is present. Twins which are both male in sex are always normal, and this again is evidence that the freemartin must be considered as genetically a female. What is it that causes the female calf twin to become intersexual? Embryological investigation gives a clear answer to the question. It shows that the two embyros develop each in a horn of the uterus, but at a very early stage the membranes grow towards the unpaired section of the uterus bicornis where they fuse so that a common Chorion results. Following on this event the blood vessels anastomose so that blood from one embryo circulates also through the other. This important point, which has been described by Lillie as well as by Keller and Tandler, is illustrated in Fig. 57 where the anastomosis of the blood vessels is shown.

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[1] Lillie, F. R., "The Freemartin ; A Study of the Action of Sex Hormones in the Fœtal Life of Cattle." Journ. Exp. Zool., 23, 1917.—Keller and Tandler, "Über das Verhalten der Eihäut bei der Zwillingsträchigkeit des Rindes." Wiener Tierärztl, Monatsschr., 3, 1916.

[2] Tandler und Keller, "Uber das Verhalten des Chorions bei verschieden geschlechtlicher Zwillingsgravidität des Rindes." Dtsch. tierärztliche Wochenschr., 19, 1911.

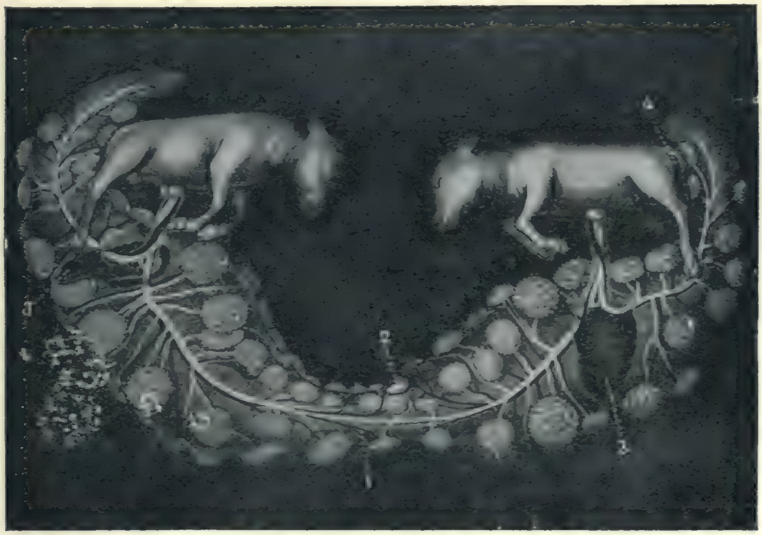

Fig. 57.—Twin embryos of cattle demonstrating the anastomosis of blood vessels at 1. After Lillie.

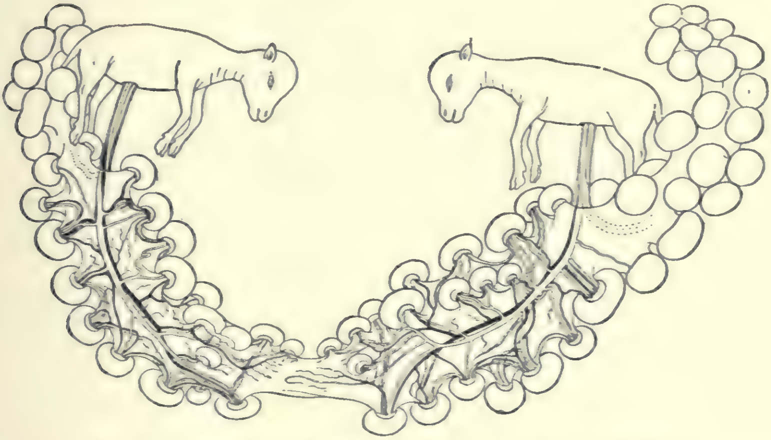

Fig. 58.—Female twins of sheep. There is no blood anastomosis. After Lillie.

If at this early stage the testes of the male twin produce hormones which determine male differentiation, they can enter the female embryo by way of the blood stream and induce intersexuality, which would be an embryonic hormonic intersexuality. Both the authors named arrived at this conclusion.

The accuracy of this conception must now be demonstrated. First we have the anastomosis of the blood vessels. It is quite evident that this is the deciding factor, because in all cases of normal sexuality there is no such anastomosis. Then again in all other mammals where twins of different sex occur there is no connection between the two embryonic circulations, as a comparison of Fig. 58 (the condition in the sheep) with the preceding illustration shows. Then there is another question—How is it that the female becomes intersexual and the male not, although the same blood runs through each? According to Lillie the answer follows from the fact that the testis differentiates histologically earlier than the ovary and its interstitial glands are ready to secrete at the time when the embryological conditions favour the action of its hormones. The result, as histological investigation shows, is that the corresponding differentiation of the ovary is actually repressed from this early stage and consequently the female hormones never come into action at all. This in itself proves that the freemartin is an intersexual female which has been produced through the presence and influence of male hormones in its blood during the time of differentiation of the sexual characters. The physiological effect of the hormones is thus the same as the abnormal concentration of the sex enzymes in the Gipsy moth experiments—a point also stressed by Lillie.

So far as details are concerned, it appears that the degree of intersexuality of the freemartin varies within certain limits, and judging by the data available the cause appears to be the same as that in the case of the gipsy moths, namely, the relation of the differentiation time of an organ to the time when the hormones commence action. The external genitalia are least often affected (sometimes the clitoris develops into a kind of phallus, Keller and Tandler), and the same applies to the mammary glands which appear to be differentiated very early. The internal organs which do not arise until later are most affected, and it is these which become almost male in the freemartin. In Fig. 59a, b, and c, three typical young embryos are illustrated, male, female, and freemartin; it will be seen how the development of the gonads in the freemartin has been repressed. Seminiferous tubules are present in the gonads later on, but spermatogenesis does not take place. In the place of the female ligamentum rotundum the male gubernaculum has developed; in one of the Keller-Tandler cases the descent of the testis had even begun. Müller's ducts have not progressed, but the Wolffian ducts are distinct. The urinogenital sinus is intermediate in condition, the phallus is mostly female in character and also the teats and the absence of a scrotum. On the whole this is the condition which endures.

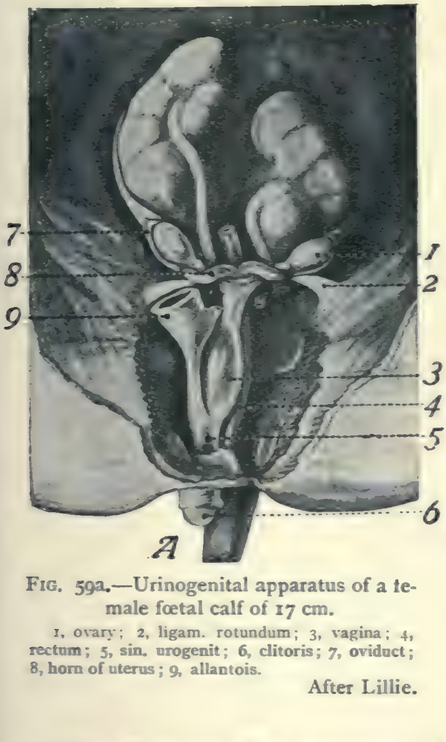

FIG. 59a.—Urinogenital apparatus of a female fœtal calf of 17 cm.

1, ovary; 2, ligam. rotundum; 3, vagina; 4, rectum; 5, sin. urogenit; 6, clitoris; 7, oviduct; 8, horn of uterus; 9, allantois.

After Lillie.

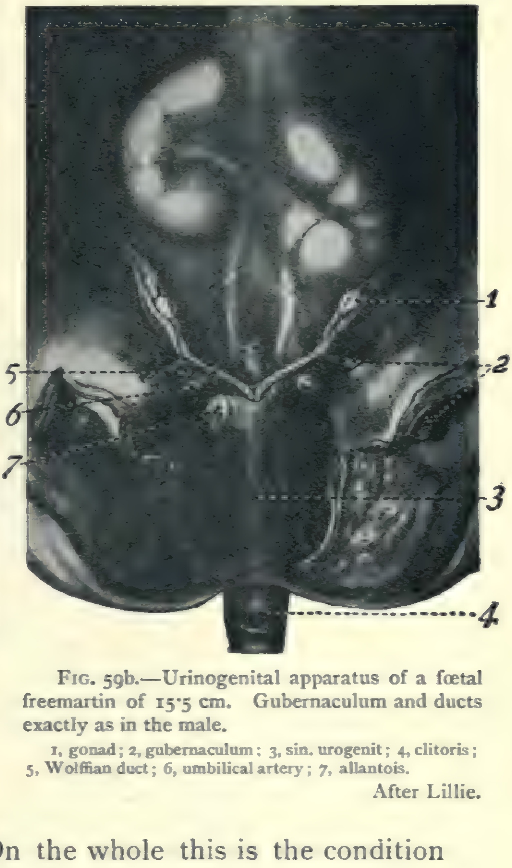

FIG. 59b.—Urinogenital apparatus of a fœtal freemartin of 15·5 cm. Gubernaculum and ducts exactly as in the male.

1, gonad; 2, gubernaculum; 3, sin. urogenit; 4, clitoris; 5, Wolffian duct; 6, umbilical artery; 7, allantois.

After Lillie.

The study of this remarkable case has given us an insight into the working of sex hormones which naturally could not be obtained from the castration and transplantation experiments on more or less fully developed animals. It has shown that real intersexuality (possibly also a complete transformation of one sex into the other, although according to Lillie no certain case is known) can be produced if the hormone action begins at the right time.

A very important experimental confirmation has just been added to these discoveries by one of Lillie's pupils, Minoura.[1] This worker transplanted small pieces of the reproductive organs of embryo and grown-up chicks on to the chorio-allantoic membrane of chick embryos of two to sixteen days. Many of these grafts healed up and attained vascular connections with the embryo. Now in some of these individuals actual modifications of the reproductive organs resulted, modifications in the direction of the opposite sex such as the retention of the Mullerian ducts, increase in size of the left testis (female birds possess only a left ovary), and conversely the retention of the right ovary in females. Thus in these experiments, so far as they go, a certain degree of hormonic intersexuality seems to have been experimentally attained.

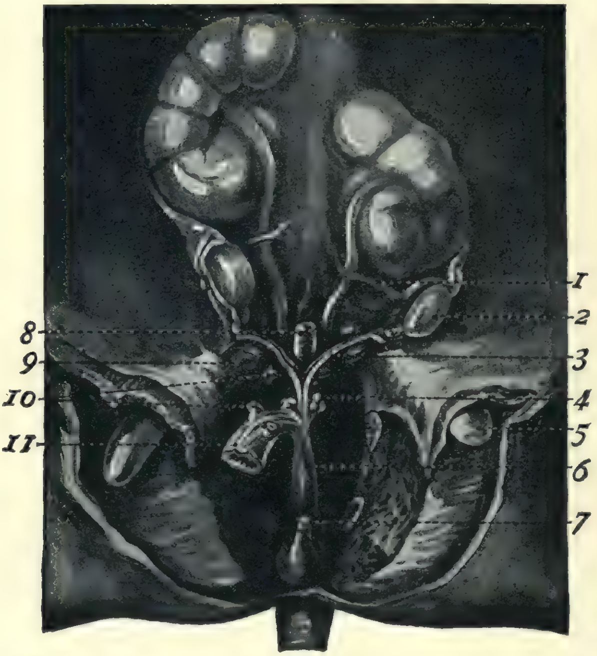

FIG. 59C.—Urinogenital apparatus of a male calf embryo of 15·8 cm. Descent of the testis not yet completed.

1, spermatic artery; 2, testis; 3, vas deferens; 4, vesiculæ seminales; 5, gubernaculum; 6, sin. urogenit; 7, root of penis; 8, rectum; 9, umbilical artery; 10, uretur; 11, allantois.

After Lillie.

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[1] Minoura, T. A., "Study of Testis and Ovary Grafts on the Hen's Egg and their Effects on the Embryo." Journ. Exp. Zool., 33, 1921.

We may add that it is not altogether improbable that other cases which have been grouped with the above, as, for example, "freemartins" by goats, are really zygotic intersexuals. With goats (particularly Toggenburg animals) the abnormality is relatively common, and cases are known here where both individuals of a twin pair are intersexual.[1] At birth the external genitals and udder are completely female, whilst internally the reproductive organs are male, although the female ducts are present in their entirety. After birth the external genitals gradually change in the male direction, and likewise the other characters of the body. Since there is a good deal of evidence that certain bucks in particular produce such offspring (for example, it is asserted that one individual produced none but intersexual offspring), it would not be surprising if this case turned out to be real zygotic intersexuality. Attempts made to invalidate Lillie's evidence by using this case (Richards and Jones) must in consequence be regarded as failures, the more so as Keller has recently demonstrated the same placental anastomosis for such goat embryos.[2]

And so we have the connection between the hormone theory and that of zygotic sex determination which is set forth comprehensively in the next section.

c. Conclusions

In order to bring the facts described above into their proper place in our general review of the sex problem, it is necessary to be quite clear as regards the relationship of zygotic and hormonic intersexuality. Now it appears to us that this relationship must be regarded as a special case of the general problem of differentiation and determination in insects and higher vertebrates. All the results of experimental embryology indicate that in the differentiation of the organs during the development two phenomena are to be distinguished. One of these is the unfolding of the inherited fundaments (*anlage*) and their correct distribution in general. The second is the realization of processes of growth which lead finally to specific form. This seems to be directed by the substances designated hormones, a fact recognized long ago by Sachs and emphasized again to-day by Loeb.[1] The punctual and specific production of these hormones is probably the duty of the hereditary factors localized in the chromosomes.[2] In animals of the insect type the hormones of definitive form and structure are evidently present in every cell, and are produced there to a great extent independently of the rest of the body. In the higher vertebrates the conditions are different and an intermediate step is interpolated, the hormone production being cared for by special organs, the ductless glands.

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[1] Davis, "Caprine Freemartins." The Veterinary Journal, 1913.—Richards, E., and Jones, J. W., "On Abnormal Sexual Characters in Twin-goats." Journ. of Anat., 52, 1918.

[2] Keller, K., "Zur Frage der Sterilen Zwillings Kälber." Wiener Tierärztl, Monatsschrift., 7, 1920.

Arguing from this to the inheritance of sex, the conditions of hormonic intersexuality show in general that the sex heredity mechanism leads to the production of hormones for the differentiation of the characters of sex. In the case of the insects intersexuality could only be obtained through abnormal zygotic constitution, because the production of hormones is not localized in special organs, but takes place within the individual cells. In the other group it is possible to obtain[3] intersexuality independent of the zygotic constitution because the hormone production is localized in organs which can be removed or transplanted, and their action independently of the zygotic constitution which originally called them forth can in this way be investigated.

The study of hormonic intersexuality, and above all the real, gives us the answer to the question which we encountered in our inferences from the study of zygotic intersexuality: What is it that the sex enzymes produce as the end products of their activity?—And the answer is—the hormones which are responsible for the modelling of definitive sexual form.

d. Appendix to Hormonic Intersexuality

Intersexuality through Parasitic Castration and the Chemistry of Sex Determination

The remarkable phenomena of parasitic castration must be taken separately because it is somewhat difficult to arrange them in the other categories. In the particular cases with which we are acquainted the nature of the gametes is not known nor has the presence of internal secretions from the gonads been demonstrated. One of the best-known examples is that discovered by Giard[1] and then more exactly investigated by Geoffrey Smith, the parasitism of crabs (*Inachus*, etc.), by *Sacculina*, one of the Rhizocephala. Such crabs when infected experience a more or less intense regression of the reproductive organs, the so-called parasitic castration. The female crabs do not react to this condition, or only to a relatively slight degree, but the males suffer a far-reaching transformation in all their secondary sexual characters, such as width and form of abdomen, shape of the chelæ, and abdominal appendages. All these structures take on the female characters. Fig. 60 illustrates the changes which take place. Perhaps the most important feature of all is that in extreme cases eggs may be developed in the testis, so that real male intersexuality is present. Smith believed that the cause of these alterations was a change in the metabolism, in particular of the fat metabolism, since this actually becomes female in type. But it is known that both in the Insects and in the Vertebrates the character of the blood as well as the metabolism is usually different in the two sexes, yet blood transfusion has no effect upon the sex. One might just as well argue therefore that this altered metabolism in the parasitized crab is likewise a transformed secondary sexual character and not the cause of such.

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[1] Loeb, J., "The Organism as a Whole." New York, 1916.

[2] See Goldschmidt in Correns and Goldschmidt, l.c.—Goldschmidt, R., "Intersexuality and the Endocrine Aspect of Sex." Endocrinology, 2, 1918.—"Die quantitativen Grundlage von Vererbung und Artbildung." (In press.)

[3] In Roux's "Aufs. Vorträge Entwicklungsmech. d. Organism," 1920.

Another case of parasitic castration is that known as stylopization in bees, discovered by Pérez.[2] A bee of the genus *Andrena* attacked by the parasitic insect *Stylops* may undergo parasitic castration, and in consequence (or perhaps it would be better to say in consequence of the presence of the parasite) some of the secondary sexual characters become transformed. The transformation in this example, however, is found in both sexes although more intensive in females. It is not far reaching in any case. Now there can be no doubt that these facts are of great significance from the point of view of the sex problem, but their analysis has not in our opinion progressed far enough to permit of definite conclusions being drawn from them. At the same time a short discussion of the possible significance of this phenomenon is necessary, for if the point of view advanced below turns out to be correct, there would be a good prospect of fitting in the keystone to the physiology of sex determination.

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[1] Smith, G., "Rhizocephala." Fauna und Flora des Golfs von Neapel. Mon. 29, 1916.—"Studies in the Experimental Analysis of Sex." Quart. Journ. Micr. Sci., V, 50, 57, 59, 1910-13.

[2] Kopeč, St., "Untersuchungen über Kastration u. Transplantation bei Schmetterlingen." Arch. Entwicklungsmech., 33, 1911.—Perez, J., "Des effets du Parasitisme," etc. Soc. Linn. Bordeaux, 12, 1885.—Smith, G., "Stylops and Stylopization." Quart. Journ. Micr. Sci., 60, 1914.

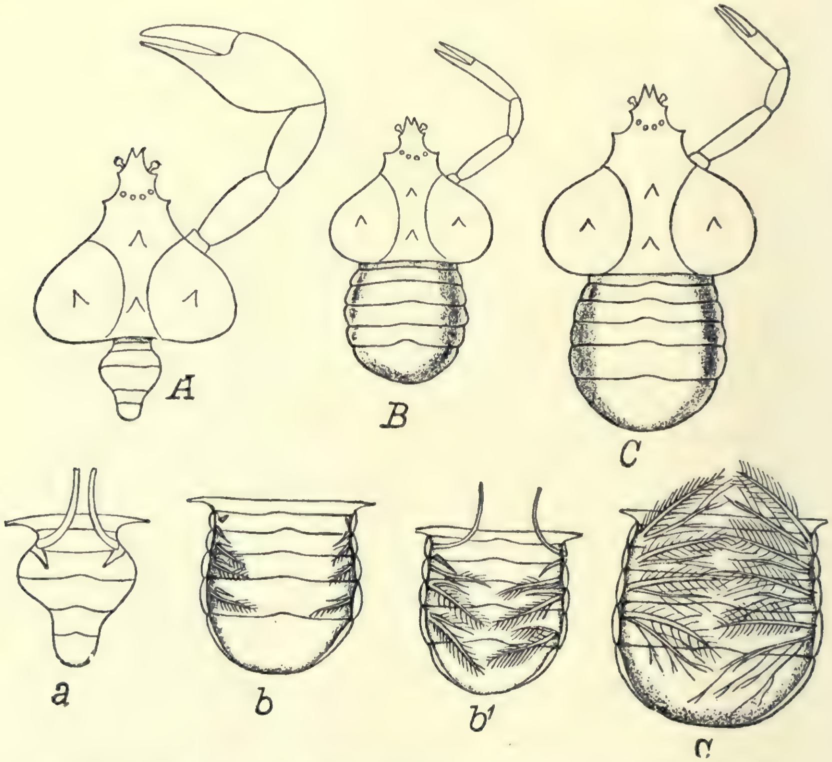

Fig. 60.—Transformation of the secondary sexual characters of the male *Inachus mauritanicus* under the influence of *Sacculina neglecta*.

After Geoffrey Smith.

A, adult normal male; a, underside of abdomen of normal adult male; B, male infected with sacculina showing complete resemblance to a female, C; b, underside of abdomen of infected male, B, showing reduced copulatory styles and swimmerets; b^1, underside of abdomen of a similar male specimen with well-developed styles and swimmerets; C, adult normal female; c, underside of abdomen of same showing swimmerets. In A, B, and C, only one chela is drawn and the thoracic limbs are left out.

From Correns.

Geoffrey Smith believed that his results demonstrated the inaccuracy of the hormone theory of sex differentiation. He was certainly limited thereby to the conditions which we have termed hormonic intersexuality, namely, the production of hormones by the reproductive organs. Zygotic intersexuality with its consequences was at that time unknown, as was also the case of the freemartin. In opposition to the theory of internal secretions Smith set up his theory of *metabolic stimuli*, his idea being that *Sacculina* (in the same way as the presence of the ovary) modified the metabolism in the direction of rich fat production. He was able to prove this effect experimentally. Since this fat is the food material of the eggs, the primordial germ cells of the parasitically castrated male were supposed to develop into eggs.

Now although there is no evidence to doubt the accuracy of these discoveries, we doubt very much whether the proper distinction has been drawn between cause and effect. An observation from our intersexuality experiments makes this very improbable. The female Gipsy moth caterpillar deposits masses of fat and in consequence the female pupa is larger than the male. During the pupal stage this fat is used up in the development of the ripe ovary which eventually fills the broad abdomen. If now in the case of medium-female intersexuality the "turning point" occurs just at the time of pupation, we obtain intersexual females with the stout female abdomen crammed with fat and its katabolic products in the form of a brown fluid, but the ovary in the midst of it remains in the caterpillar condition (except that histologically it shows signs of transformation into a testis). The food material of the egg is there, but the influence of the male hormones has prevented its use. The production of fat in the case of *Sacculina* can hardly be accepted then as the cause of the intersexuality, rather is it due to the action of something else yet unknown. This might perhaps be the repression or compensation of the male hormone production through the presence of the parasite.

Nevertheless we believe that there is a nucleus of truth in Smith's idea when freed from the exaggerated criticism of the hormone theory.

The facts previously considered have brought us to the point where the hormones of sex differentiation commence their activity. In regard to the mode of action of these bodies we have so far formulated no idea. Naturally there is nothing mystic about it, it is a chemical process and more than likely after all an action on the general metabolism. The action of the hormones probably calls forth a specific type of metabolism, and this is the ultimate and direct cause of the morphological differentiation of the sexes.

If this were correct it would be the last word in the elucidation of the sex problem, and at the same time one which could be subjected to exact analysis.

To what extent then do the facts permit us to draw a conclusion of this kind? There is scarcely any need for a special discussion in order to show that hormones in general exert specific influences on the metabolism. The action of the pancreatic and thyroid hormones on the carbohydrate metabolism is well known, as also the influences of hormones on growth and processes of differentiation shown by experiments with thyroid and hypophysis. How does the matter stand, however, in regard to the relation between metabolism and differentiation on the one hand and metabolism and sex on the other? So far as the first point is concerned we already possess some very important information, the researches of Weinland[1] in particular furnishing us with data. This investigator demonstrated that dipterous larvæ excreted large quantities of ammonia and amines whilst the pupæ produced no volatile nitrogenous substances except uric acid as the end product. The life processes of the larvæ were therefore of a different chemical order from those of the pupæ and the adult flies. This also agrees with the fact that the larva and imago partake of different food, just as the omnivorous tadpole metamorphoses into the carnivorous frog with a complete change in form and chemistry. Now the point is whether the change in form determines the alteration in the chemical processes or *vice versa*. Weinland refers first to observations on internal secretions which show that an alteration in chemical action can determine change of form. As an example he brings forward the observation of Born that the metamorphosis of fused double larvæ of the frog takes place simultaneously independently of the size. In the meantime the experiments of Gudernatsch have shown clearly the influence of thyroid gland extracts on the metamorphosis of Amphibia, and Uhlenhuth,[2] with very beautiful experiments, has demonstrated the influence of hormones on the metamorphosis of amphibian skin transplanted to larvæ of different age. These experiments lead to the same conclusions as those of Born.

Now it is well known that the metamorphosis of the Diptera begins with the complete destruction of the larval tissues and the simultaneous development of the imaginal discs. "It is probably not feasible to assume a morphological cause, but very tempting to look for the cause in an alteration of the chemical processes which attracts the phagocytes to the destructible tissue; it might be occasioned by the prolonged period of hunger at the end of the larval life which determines some other mode of tissue nourishment; it might be due to other factors such as alteration in available oxygen, or the CO_2 content of the environment, etc., when the flesh which has been the normal habitat up to this period is left"—Weinland. Since, however, the alteration in the nitrogen metabolism is not a gradual one, but occurs suddenly with the pupation, one must conclude that it is the cause of the change in form.

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[1] Weinland, E., "Über die Stoffumsetzungen während der metamorphose der Fleischfliege" (*Calliphora vomitoria*). Zeitschr. Biologie, 47, 1906.

[2] Uhlenhuth, E., Journ. Exp. Zool., 1918.

How can these views be applied in connection with sex differentiation? Do they make it more probable that a specific type of chemical change occurring at some particular moment is responsible for sex differentiation? One must first enquire how far a chemical difference goes hand in hand with sexual difference. As a matter of fact this has often been demonstrated, and for exactly the same or similar objects as those which have supplied us with important data regarding sex determination. Geoffrey Smith, for example, showed that in female crabs with ripe ovaries the blood is saturated with fat and lutein and appears yellow in consequence, whilst the fat production of the male is much less and the blood is pink in colour.

Analogous conditions are stated to hold good for plant-eating insects (Steche[1] and Geyer), including the Gipsy moth. In these cases the blood of the female is green through the presence of but slightly altered chlorophyll, whilst in the male it is yellow in consequence of the xanthophyll contents. More exact quantitative results are also forthcoming which will be of the greatest importance in future studies. Thus Farkas[2] has stated that in the case of the silkworm the body weight of the female is not only absolutely higher than that of the male, but also relatively, that is compared with the original weight of the caterpillars. The proportions are 29·1 : 22·1 per cent. The female moth contains on an average 1523 calories of energy, the male 985 ; the specific energy content of the dry substance of the male is 6411 calories, of the female 5976. During the pupal stage the male pupæ lose 14·3 per cent of their substance, the female 12·4 per cent. In fact the male caterpillars use more substance and more energy than the female during a definite period—and for every gramme of substance used the male consumes 7·024 calories and the female 6·620.

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[1] Steche, O., "Beobachtungen über Geschlechts-unterschiede der Haemolymphe von Insektenlarven." Verh. Deutsch. Zool. Ges., 1912.—Geyer, K., "Untersuchungen über die chemische Zusammensetzung der Insektenhaemolymphe." Ztschr. wiss. Zool., 105, 1913.

[2] Farkas, K., "Beiträge zur Energetik der Ontogenese, III." Pflüger's Archiv., 103, 1898.

Thus there can be no doubt that metabolic and energetic processes are different in the two sexes. The discoveries of Straus[1] in his work on bees are also in agreement with the conclusions arrived at above. Figs. 61 and 62 present the curves for the fat and glycogen content of worker bees and drones during the development. They show quite clearly the difference between the two in so far as the metabolism of reserve materials is concerned.[2]

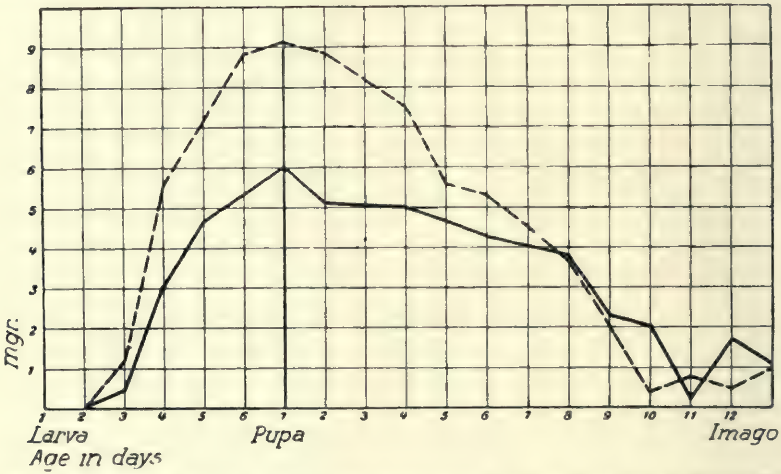

Fig. 61.—Alteration in the fat and glycogen contents of bee workers during development.
.... glycogen ——— fat After Straus.

It would be necessary now to bring into relationship the different chemistry with the time point of sex determination, in order to demonstrate the accuracy of the views from which we started. Unfortunately this has not yet been done, but it could be carried out. One fact towards it is provided in the discovery of Smith that the parasitically castrated crab with the female sex characters assumes also the female type of metabolism. His conclusion that the parasitism was responsible for the chemical change in the metabolism of the crab, which in turn influenced the sex characters, was really the starting point of these observations. Other facts may be deduced from our intersexuality experiments, as for example the observation that the production of the chromogen for the wing pigment in male intersexuality ceases with the "turning point"—further information of a more indirect nature can also be brought forward.

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[1] Straus, J., "Die Chemische Zusammensetzung der Arbeitsbienen und Drohnen." Ztschr. f. Biologie, 56, 1911.

[2] See also Lawrence, J. V., and Riddle, O., "Studies on the Physiology of Reproduction in Birds." Journ. Phys., 41, 1916.—Lipschütz, A., "Körpertemperatur als Geschlechtsmerkmal." Anz. Ak. Wiss. Wien., 1916.

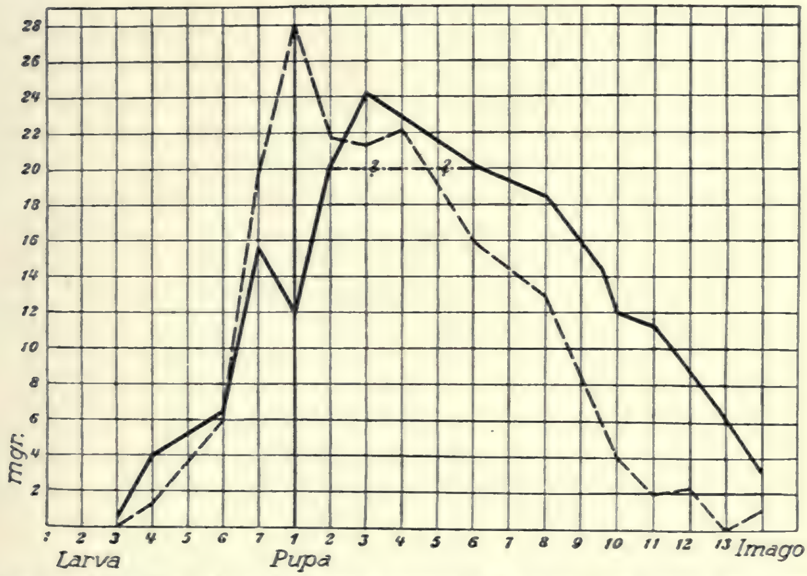

FIG. 62.—Alteration in fat and glycogen contents in the drone bee during development
.... glycogen ——— fat. After Straus.

A further glimpse into these conditions may perhaps be obtained from quite another side. The growth of eggs within the destroyed testis of the parasitized crabs is really a process of regeneration. Now there are one or two indications that occasionally the chemical changes which may go hand in hand with regeneration bring about similar results. For instance Braem[1] has stated that after excision of the genital

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[1] Braem, F., "Zur Entwicklungsgeschichte von *Ophryotrocha puerilis*." Ztschr. wiss. Zool., 57, 1894.

segments of a female *Ophryotrocha* the regenerated piece produces sperm cells. And Meyers[1] finds that after transplantation of frog testes the tissues often degenerate, after which new growth takes place in which egg cells are formed adjacent to the sperm cells.

We maintain therefore that the facts discussed here are not opposed to our former deductions—on the contrary they are not only in agreement with the conclusions hitherto reached, but are apparently calculated to clinch those conclusions by physiological arguments.

Here might be added yet another small observation which is perhaps not without importance. In insect metamorphosis the alteration of the chemical processes coincides with the beginning of an extraordinary phagocytosis, as Weinland has pointed out. Now in intersexual frogs (of which we shall hear more later) a phagocytosis of the eggs may take place when the ovary undergoes transformation into a testis (Schmitt-Marcel), and we shall see that the same is true of parasitic Crustacea.

In the same way during the transformation of the ovary into a testis in the case of intersexual female Gipsy moths an extraordinary phagocytosis takes place. These facts are sufficient to show that it is proper to utilize in this place the point of view taken up by Weinland.

Finally it may be mentioned that both Geoffrey Smith and Geyer found, in regard to the precipitin reaction, that both sexes of a species stood to one another as different species. From this also important information may possibly be obtained.

4. Intersexuality Through Activation

To this group, the designation of which will be upheld later, belongs the extraordinarily important case of sex determination in *Bonellia.* This worm has for a long time been regarded as the typical example of the most extreme sexual dimorphism. The female is a worm of the size of a plum, with a proboscis almost a metre in length, the male, on the other hand, is a minute creature of a few millimetres which passes its life in the uterus of the female. The extremely important investigation of sex determination in this worm was carried out by

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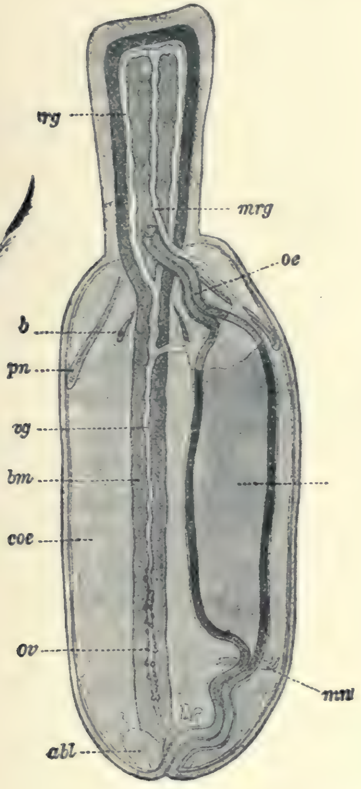
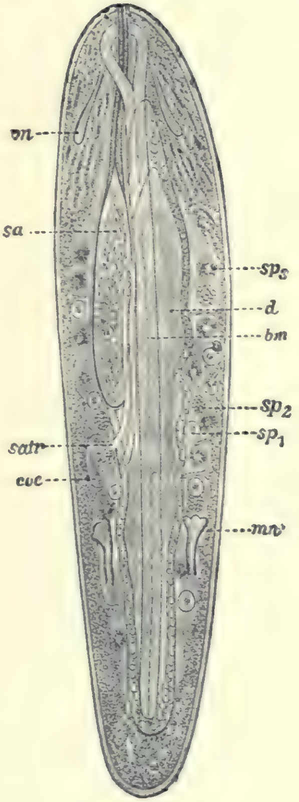
[1] Meyers, R., "Transplantationen jugendlicher und erwachsener Keimdrüsen usw." Arch. Mikr. Anat., 79, 1912.

Baltzer,[1] the chief results being the following: All the embryos on hatching have the power of becoming either males or females. If an embryo is in a position to attach itself to the proboscis of an old female it does so, and then passes through a kind of parasitic development there for a time during which metabolic relations exist in all probability between larva and proboscis. Every larva which does this develops into a male. On the other hand, if a larva does not attach itself to a female, it remains for a time indifferent in sex. Eventually, however, the majority of



a.



b.

FIG. 63a.—Young ♀ *Bonellia* shortly after metamorphosis.

Abl, anal vesicles; b, setae; bm, nerve cord; cœ, cœlom; d, mid gut; mn, metanephridia; mrg, middle proboscis vessel; œ œsophagus; ov, ovary; pn protonephridia; srg, lateral proboscis vessel; vg, ventral blood vessel.

FIG. 63b.—♂ *Bonellia*, sexually mature. References as before, also sa, sperm reservoir; satr, funnel of sperm reservoir; sp_{1-3}, stages in spermatogenesis.

After Baltzer.

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[1] Baltzer, F., "Die Bestimmung des Geschlechts nebst einer Analyse des Geschlechtsdimorphismus bei *Bonellia*." Mitt. Zool. St. Neapel, 22, 1914.

these free individuals develop gradually into females. Suppose now that the larvæ are permitted to attach themselves to a female and then the period of parasitism is interrupted before its normal termination, the result will be intersexual individuals, the character of which is more male or female according to the length of their period of parasitism. The main facts are illustrated in Figs. 63 and 64; Fig. 63, a, is a young female bred from

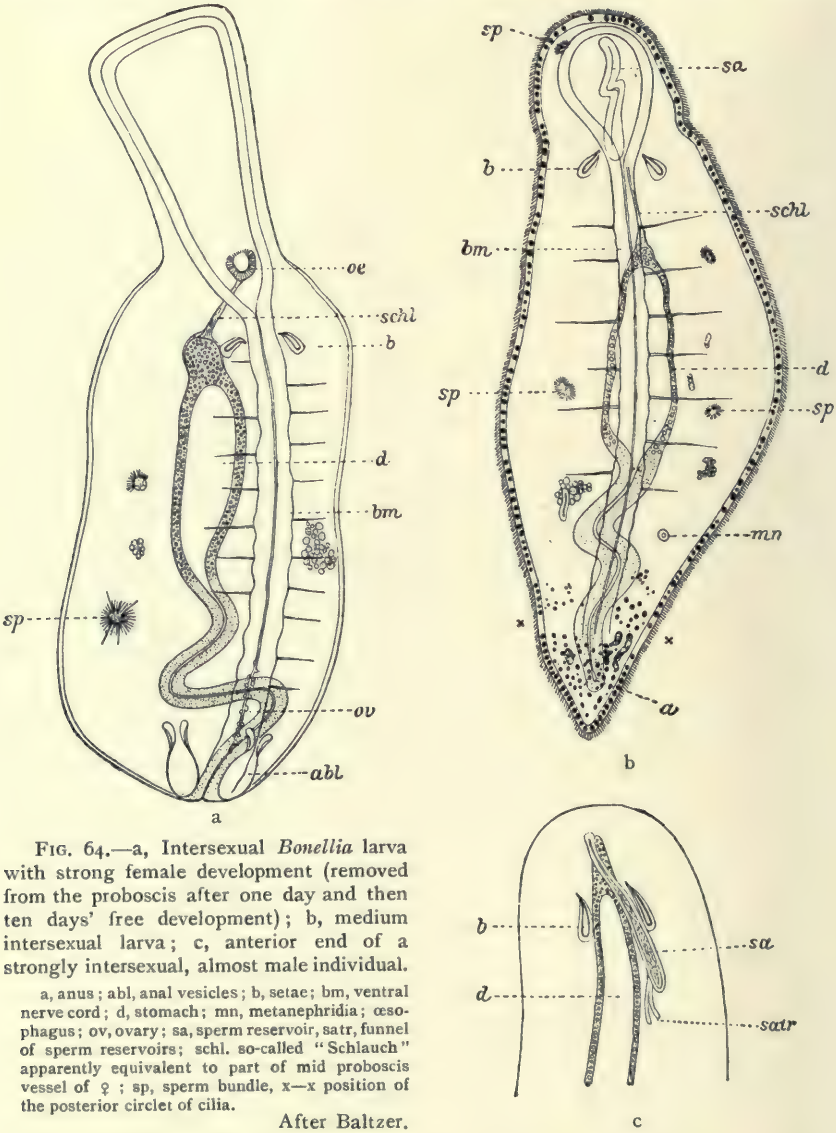

FIG. 64.—a, Intersexual *Bonellia* larva with strong female development (removed from the proboscis after one day and then ten days' free development); b, medium intersexual larva; c, anterior end of a strongly intersexual, almost male individual.

a, anus; abl, anal vesicles; b, setae; bm, ventral nerve cord; d, stomach; mn, metanephridia; œsophagus; ov, ovary; sa, sperm reservoir, satr, funnel of sperm reservoirs; schl. so-called "Schlauch" apparently equivalent to part of mid proboscis vessel of ♀; sp, sperm bundle, x—x position of the posterior circlet of cilia.

After Baltzer.

the egg stage. The characteristic features are the proboscis at the anterior end and the presence of a complete alimentary canal with œsophagus and anus. At the sides of the latter lie the anal vesicles. Posterior to the proboscis are two typical setæ and on the wall of a ventral blood vessel the ovary develops. The young male (Fig. 63, b) is quite different in appearance. Œsophagus and anus are both missing and also setae and proboscis, whilst the sexual organs in the form of two seminal vesicles, sperm funnels, and the germinal cells along the coelomic wall are well developed. Fig. 64, a, depicts an intersexual individual which is still strongly female. One notices the rudimentary œsophagus and the presence of spermatozoa. Fig. 64, b, illustrates the appearance of an intersexual individual which is more intermediate; there is no œsophagus, nor are there any anal vesicles; the sperm duct is present and also spermatozoa. Finally in Fig. 64, c, we have the anterior end of an intersexual individual which is strongly male in character.

To appreciate these facts from the point of view we have attained in the preceding sections a few more details are necessary.

1. It is important to remember that males as well as intersexual individuals can arise in small numbers without the larvæ being parasitic on the proboscis of the female at all, and not all the parasitic larvæ which are separated again become intersexual, some become males.

2. Amongst the larvæ which develop into females those which develop late produce spermatozoa first before they become purely female.

3. A short period of parasitism accelerates development, even if it be female development.

4. The combination of male and female organs in the intersexual individual is not arbitrary. It appears to depend on the degree of differentiation of the different organs in the direction of one sex when the stimulus occurs which swings development over towards the opposite sex type.

Bearing in mind the facts of zygotic intersexuality it will be realized that we have a parallel to the last statement which encourages us to look for a common explanation. We have seen in the case of *Lymantria* that a relationship existed between the time of differentiation of an organ and the degree of intersexuality. We now observe the same condition here although perhaps not quite so distinctly. Let us turn back therefore to the relations described on p. 94 as existing between the hormone curve, the valency of the sex factors, and the intersexuality, and bring these facts into conjunction with the point stated above that the secretion of the *Bonellia* proboscis accelerates the differentiation speed of the larvæ independently of the forthcoming sex. It may be possible then to come to some understanding of the remarkable sex conditions of *Bonellia*. If we were anxious to carry out a decisive experiment to test the accuracy of our conception of zygotic intersexuality, it would be initiated with a view to discovering a method permitting us to accelerate or retard the velocity of differentiation and growth without influencing the reaction velocity of the sex enzymes. This would mean the shifting of the line S—S in Fig. 51 to left or to right. One could make either sex intersexual according as one brought the processes of differentiation into the period of action of one or the other sex enzymes. It would lead to the same consequences as the abnormal quantitative combinations in zygotic intersexuality. As a matter of fact the first steps in the direction of making such an experiment have been now accomplished, for by the action of low temperatures we have been able to attain the first stages of female intersexuality with pure female Gipsy moths. Now it appears that this experiment can also be carried out by *Bonellia*. The explanation of the *Bonellia* case may be stated as follows: The relation of the reaction velocity of the sex enzymes to the differentiation velocity of the organs is apparently such that a very slow differentiation of the organs is opposed to a sex enzyme combination in which there is great concentration of the male enzymes and less of the female. In normal development the differentiation point for most of the organs would occur beyond the point at which the female enzymes came into action and the resulting individual would be female. Only those organs which differentiated before this point would be male in character; this would explain the transitory male reproductive organs of many larvæ. The action of the proboscis secretion (analogous to that of thyroid extracts in frog metamorphosis) is to accelerate the speed of differentiation of the organs to a remarkable degree. Now if the reaction velocity of the sex enzymes remains unaltered, practically all the differentiation will take place within the period of activity of the male enzymes, and so males only will be produced. This idea is represented graphically in Fig. 65 which is modelled on the curve already discussed in

Fig. 51. The illustration shows the curves for the male and female enzyme reactions and the different differentiation velocities which result in females, males, and intersexes. A reference to the earlier curves and their explanation will suffice to make this one clear. There is no need to enter into further details, and it would be necessary to know beforehand whether in *Bonellia* one sex were heterogametic or not. The complete explanation, especially of the exceptional males which develop without parasitism, is impossible without such knowledge, and this is not forthcoming at present. There is a further possibility and that is that all the *Bonellia* are genetically males (we shall see later that this is so in a related case, where parasitic crustacea are concerned). This would simplify still further the above view, for everything would take place within one sex formula.

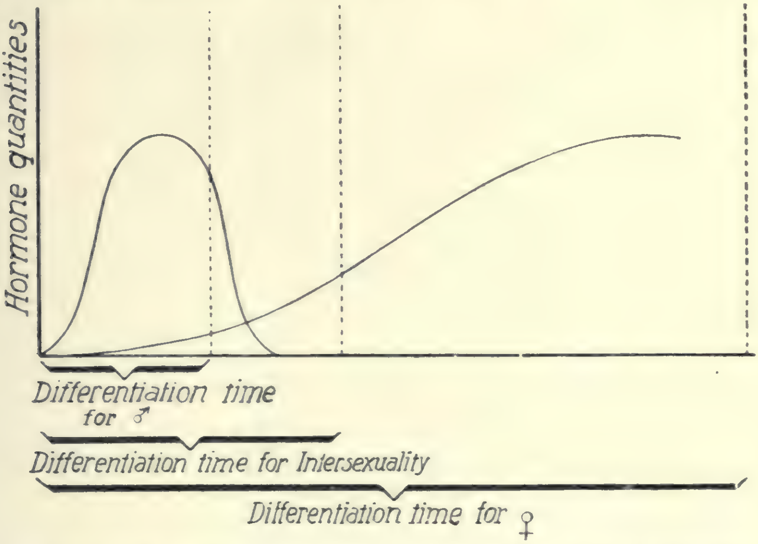

FIG. 65.—Graph illustrating the interpretation of Baltzer's *Bonellia* experiments.

A word or two may perhaps be added in regard to the remarkable secretion of the *Bonellia* proboscis which by accelerating the speed of differentiation leads to intersexuality through activation (the title to this section is explained hereby). It is natural to compare this secretion with the action of known hormones, in particular with the action of thyroid and hypophysis hormones on Amphibia. Thus the thyroid hormones bring about metamorphosis of frog tadpoles, that is to say differentiation, independently of growth. The hypophysis hormones act in an almost opposite manner on the same animals. The action of the *Bonellia* secretion appears no longer remarkable when it is seen that in these examples feeding with the ductless gland in question is sufficient to bring about the typical results.

5. Transitory Intersexuality

The phenomena that we arrange under this heading are best exemplified by the peculiar sexual conditions of the frog. Pflüger in 1882 discovered the remarkable fact that very young frogs which came from different localities presented quite different sex ratios. Whilst specimens from Königsberg gave the normal sex ratio of 1 : 1 males and females, collections from Utrecht were largely female, the proportions being 87 ♀ : 13 ♂. Adult frogs, however, from both localities gave the normal relations of the sexes. Pflüger assumed that a certain number of the young Utrecht females must change into males as they grew older. And as a matter of fact he discovered eggs in the testes of three-year old Utrecht males, and came to the conclusion that in the young stages of the frog there were three kinds of individuals, females, males, and hermaphrodites, the latter changing in the course of their development into males or females. More recently R. Hertwig with his pupils Schmitt-Marcel, Kuschakewitsch, and Witschi[1] have again taken up the problem and investigated it from both the experimental and embryological sides.

The most important facts which enable us to bring the explanation into its correct position in the general sex problem are the following: The frog presents two chief forms in regard to the development of the reproductive organs, and these are usually found in geographically separated races. In the one type the differentiation of the sexes is normal and takes place early, the reproductive organs are either male or female from the beginning. In the other type all the reproductive organs are at first female in character and sooner or later 50 per cent become transformed into testes. In this latter case there are all kinds of quantitative variations and variations in time. The development may be sketched as follows. In every young larva a gonad develops which may be termed indifferent in character. It consists of a ridge of germ cells, in the middle of which a cavity arises—the primary genital cavity—the wall of which is formed of the germ cell epithelium. Segmentally arranged strands of cells, the genital strands, grow into this cavity from the base of the genital fold. A transverse section through such a gonad looks like the illustration depicted in Fig. 66 (see Figs. 70 and 71 for diagrams). If such an organ develops into an ovary the primordial germ cells increase in number and form characteristic egg nests, in whose cells the usual synaptic processes take place. Very soon the growing oocytes are clearly differentiated and yolk formation commences. The genital strands, however, are of little importance in the ovary and gradually become transformed into the ovarial pouches. Figs. 67 and 68 are stages in the development the continuation of which does not present anything of special interest.

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[1] Hertwig, R., "Über den derzeitigen Stand des Sexualitätsproblems nebst eigenen Untersuchungen." Biol. Centrbl., 32, 1912. The older Literature is cited here.—Kuschakewitsch, S., "Die Entwicklungsgeschichte der Keimdrüsen von *Rana esculenta.*" Festschr. f. R. Hertwig. Jena, 1910.—Schmitt-Marcell, W., "Über Pseudohermaphroditismus bei *Rana esculenta.*" A. Mikr. An., 72, 1908. —Witschi, E., "Die Keimdrüsen von *Rana temporaria.*" *Ibid.*, 85, 1914. —"Studien über Geschlechtsbestimmung bei Fröschen." *Ibid.*, 86, 1915.

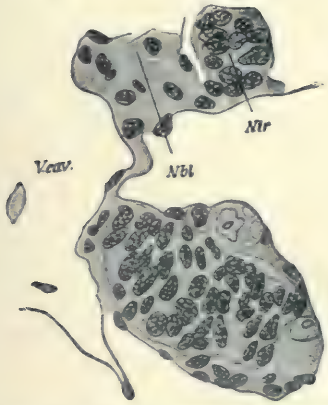

FIG. 66.—Young stage in the development of the indifferent gonad of *Rana temporaria.*

Nbl, nephroblasts; Ntr, nephrostome; V. cav., vena cava.

After Witschi.

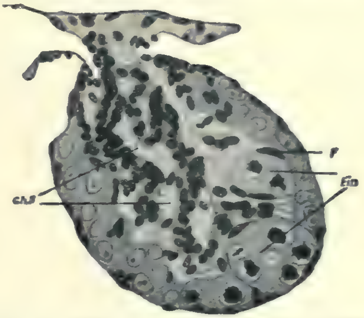

FIG. 67.—*Rana temporaria.* Young ovary.

Ein, egg nest; F, follicle epithelium; Gh II., secondary gonad cavity.

After Witschi.

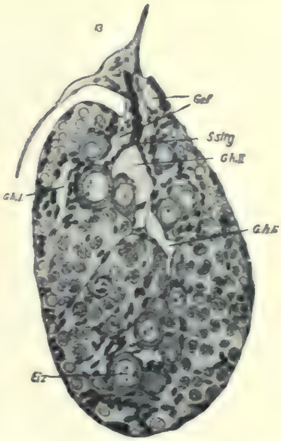

FIG. 68.—*Rana temporaria.* Somewhat older ovary.

Ein, egg nest; Gef, blood vessel; Gh I., primary; Gh II., secondary gonocavity; Sstrg, sexual strand (sex cord).

After Witschi.

The development of the testis from the indifferent gonad runs somewhat differently. The gonocytes leave the germinal epithelium and become applied to the genital strands. Fusion takes place between the nests of germ cells and the wall of the genital strands and then each nest develops a cavity or ampulla (the testis ampulla or sperm canal, since they soon lose their vesicular form and become tubular).

The germ cells increase constantly in number, but the synaptic phenomena do not take place until the fourth year. This only applies to *Rana temporaria*. In other species it begins earlier. By means of special outgrowths the well-known connections between the genital strands and the pronephros are constituted. Fig. 69 is a transverse section through such a young testis; it can be compared with the figures of the developing ovary. The latter development is illustrated diagrammatically in Fig. 70. The indirect testicular development, that is to say, the later transformation of an ovary into a testis, may take place at different stages. The transformation begins in

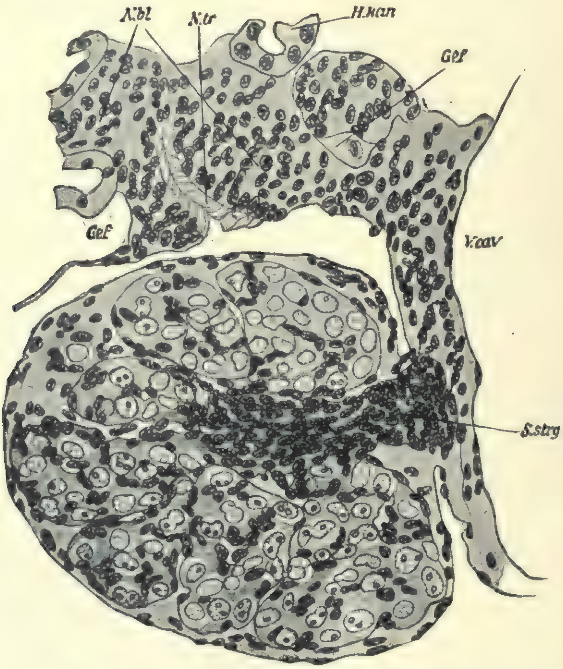

FIG. 69.—Stage in the direct testis development of *Rana temporaria*.
Gef, blood vessel; H, kan, kidney duct; Nbl, nephrotome cells; Ntr, nephrostome; Sstr, sexual strand; V. cav., vena cava.

After Witschi.

many types in the late larval period, occasionally, however, after sex maturity has been reached. In the latter case the individuals which are found in the process of transformation are the so-called adult hermaphrodites. (It may be added that there are other adult hermaphrodites which are genetically females, see later.)

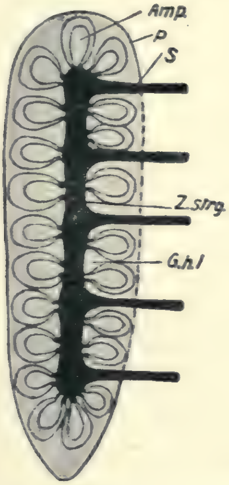

FIG. 70.—Diagram of a young frog testis where the development is direct.

Amp, testis ampulla; Gh I., primary gonad cavity; P, peritoneum; S, sexual strand Zstr, central sexual strand.

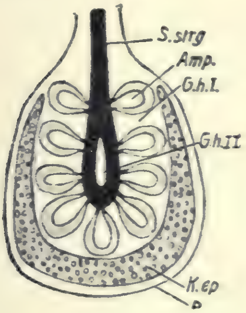

FIG. 71.—Diagram of young testis from a Pflugerian hermaphrodite.

Amp, testis ampulla; Gh I., primary, Gh II., secondary gonad cavity; Kep, female germinal epithelium; P, peritoneum; Sstr, sexual strand.

After Witschi.

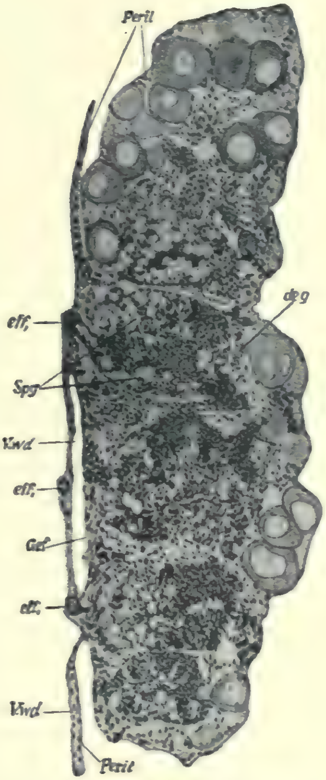

FIG. 72.—Gonad of a young frog, indirect testis development (transformation).

deg, degenerating elements; eff, vasa efferentia; Gef, blood vessel; Perit, peritoneum; Spg, spermatogonia; Vwd, wall of vena cava.

After Witschi.

The essential facts of the indirect development are as follows: The germ cells lying at the periphery of the ovary become free and wander towards the genital strands, from which, in the centre of the gonad, a real testis development takes place. Consequently at this stage the gonad is centrally a testis but peripherally an ovary, as is indicated in the diagram, Fig. 71. The female part of the organ now gradually degenerates, and only in rare cases do eggs remain which maintain themselves and develop up to maturity in the completed reproductive organ (cf. adult hermaphrodites above). Fig. 72 represents the characteristic appearance of a reproductive organ in the course of this transformation.

The way to an understanding of these embryological facts was opened up by the experimental studies of Hertwig and his pupils. A comprehensive review is, however, not easy, for difficulties of technique are responsible for gaps in the experimental series, and moreover the actual determination of the conditions of a gonad at a particular stage makes it impossible to know what the later fate of the organ might have been. Since the ovaries which have been retarded in development—Hertwig's indifferent gonads—may proceed either to fuller development or change into testes, the discovery of nothing but indifferents in an experiment is equivalent to a definite result such as the occurrence of nothing but males, females only, or both sexes in some particular ratio.

Naturally it is possible, now that the principle of the results is as we believe understood, to carry out an investigation which would escape these difficulties. It has not yet been done, however, and so we must endeavour to abstract what is of importance from the general form of the results.

In making the crosses it became evident that the tendency (which is inheritable) to direct the development along the line of early differentiation of the sex, or to direct the development with late differentiation along the path of a sex transformation, could be determined either by the hereditary nature of the father or by the mother. One and the same female crossed with different males, and also one and the same male crossed with different females, gave different results. The following table is an example:—

1. $\frac{\text{♀}\,\alpha \times \text{a}\,\text{♂}}{\text{♀} + 64\text{J} + 3\,\text{♂}}$ 2. $\frac{\text{♀}\,\alpha \times \text{♂}\,\text{b}}{69\text{J} + 54\,\text{♂}}$ 3. $\frac{\text{♀}\,\alpha \times \text{♂}\,\text{d}}{50\,\text{♀} + 52\,\text{♂}}$

4. $\frac{\text{♀}\,\beta \times \text{♂}\,\text{a}}{109\text{J}}$ 5. $\frac{\text{♀}\,\beta \times \text{♂}\,\text{b}}{34\,\text{♀} + 52\,\text{♂}}$ 6. $\frac{\text{♀}\,\beta \times \text{♂}\,\text{d}}{142\,\text{♀} + 140\,\text{♀}}$

Females and males of the same race are denoted with the corresponding Greek or Roman characters. The female *α* produces with the male a of its own race (Table Equation No. 1) almost nothing but indifferent or intermediate individuals of which the half would become transformed later into males. With the male b (Table 2), the same female produces early sex differentiated males and a lot of undifferentiated individuals which later on will become females. With the male d (Table 3), however, this same female *α* produces normally differentiated sexes.

But the female *β* crossed with the male d (No. 6) gives the same result as the female *α* crossed with this male (Table 3), whilst the cross with the male b (Table 5) is quite different from the female *α* crossed with the same male (Table 2).

Now if these results are considered one is struck at once with the resemblance to the case of zygotic intersexuality in *Lymantria dispar* which has been discussed in detail. In the first place there is nothing to prevent one regarding the intermediates as temporary intersexes. Their zygotic nature may be deduced firstly from the fact that some races produce these forms, others do not, and secondly, from the fact that with animals of different races crosses give different results. In both cases the visible phenomena are closely connected with the presence of different geographical races together, and in both cases the hereditable constitution of each of the two sexes is answerable for the result. For this reason we have tried to explain the frog results on the same lines as *Lymantria dispar*, that is by means of the principle of the different valency of heredity factors.[1] Witschi has fallen in with this scheme, and worked out his own formulæ which differ somewhat from ours.

These formulæ appear rather complicated owing to the fact that different values must be assumed for the factors for maleness as well as for the factors for femaleness in each race. Since, however, we only require the principle of the interpretation, in particular the side dealing with the physiology of development, in order to classify the case in our general statement, we need not go into these details here.

The next thing is to determine which sex is the heterozygote in the normally sex differentiated races. The question has been answered by Witschi[2] who was able to obtain an adult hermaphrodite (see above) whose eggs and sperm cells could be used for different crosses. It was possible to repeat the classical crossing experiments made by Correns on *Bryonia dioica* and *B. monoica.* The eggs of the hermaphrodite fertilized with the sperms of a race with early differentiated sexes gave both sexes; on the contrary the eggs of an early differentiated female fertilized by the sperms of the hermaphrodite gave only females, a result previously obtained by Crew.[1] It follows that the hermaphrodite is genetically female, and that the female is homozygotic, the male heterozygotic. The formulæ would therefore be (M)Ff = ♂, (M)FF = ♀. It is not necessary to detail the explanation in Mendelian symbols. Witschi has carried this out in an ingenious manner.

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[1] Goldschmidt, R., "Einführung in die Vererbungswissenschaft," 2 Aufl., 1913.

[2] Witschi, E., "Über die Genetische Konstitution der Froschzwitter." Biol. Centralbl., 1923.

We may remind the reader that we were in a position to replace the symbolic valency of hereditary factors by the concrete idea—concentration of a sex enzyme. It will now be seen that in Hertwig's results there is the same important time factor which permitted us to draw our conclusions in the Gipsy moth example: The intermediates are of different grades according to the time which elapses before transformation into males takes place. The sexually normal races are those in which the sexual differentiation takes place very early in point of time, whilst the indifferents (intermediates) indicate a very late differentiation.

To explain these conditions let us use a similar graph (Fig. 73) to that employed previously for the Gipsy moth and for *Bonellia.* The curve refers only to the males and demonstrates the conditions for a given differentiation time, the end of which is marked by the line S—S. The continuous lines, M and F, are the curves of hormone production for normal males, the dotted lines are the M-curves for different types of intermediates, the F-curve remaining the same. (M is the curve of the production of male enzyme and F of the production of female enzyme.)

Other combinations can be had through the other variable, the position of the line S—S, that is, the point where differentiation comes to an end. This no doubt is the essential explanation of the experiment. We cannot deduce all the details, however, since all the variables of this scheme may be concerned in the final result. The concentration of both M and F may be different; the point S—S at which determination is finished may be reached at different times in different races, and the form of the growth curves can be quite different. As the experiments made so far supply no exact information concerning these points, there is no reason to go into further details. It is sufficient to have established that this transitory hermaphroditism is a particular form of zygotic intersexuality. There is scarcely any need to point out that the non-participation of the secondary sexual characters in the case of early transformation of sex is due to the fact that they are only developed after the sexual determination is completed. In the adult hermaphrodites, however, the secondary sexual characters are found participating.

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[1] Crew, F. A. E., "Sex Reversal in Frogs and Toads." Journ. of Genetics, 11, 1921.

One other detail may be referred to here. It appears that in the frog we have material with which a deeper experimental insight into the physiology of intersexuality can be obtained. Hertwig and Witschi were able to show that the temperature had a very definite influence on the results of the experiment, and the different races actually react differently to the same conditions. There are forms, for example, which when cultivated at 21° give normal sex ratios in which the sexes differentiate quite early. Cultivated at 27°, however, some females change after the metamorphosis into males. In another race normal sex ratios were the rule when the animals were cultivated first at a low temperature and then at a higher, but the males were transformed from intermediates. This race, cultivated at 20°, gave exclusively females. On the other hand, from such a race nothing but males could be obtained, through the transformation of all the females, when they were bred at a temperature of 27°.

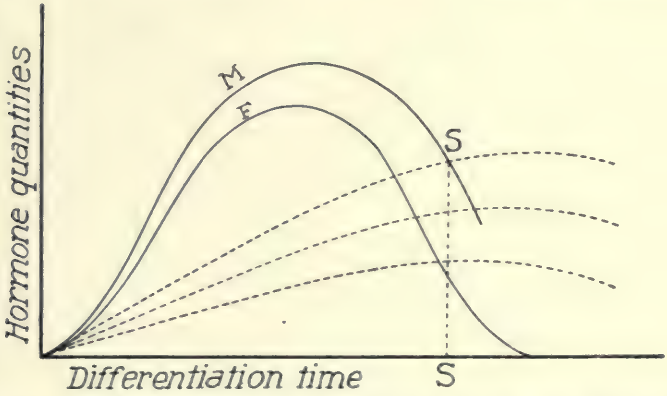

FIG. 73.—Diagram illustrating the interpretation of Hertwig's frog experiments.

These results clearly indicate the possibility of regarding the conditions explained in the above curves from the physico-chemical point of view. We shall see later in discussing Hermaphroditism that there is quite a series of observations which fall into the same category.

It ought, perhaps, to be mentioned in concluding this section that a disbelief altogether in the existence of transitory intersexuality in the frogs has been expressed and another way suggested for explaining the pictures of gonad transformation (Swingle[1]). This attempt, which rests on the basis that the author investigated very early sex differentiating forms and never saw the typical pictures of transformation, must be regarded as a complete failure.

Appendix to Chaps. II and III

Conclusions

We have designated the facts discussed in the previous pages with the title Basic Facts, for we believe that in principle they have provided the solution to the problem of the determination and heredity of sex. Put in a few words this solution is as follows : Every developing individual of a bisexual organism contains the substances whose action can call forth the one or the other sex.

A particular mechanism, disclosed by Mendelian experiments and visible in the sex chromosomes, distributes these substances to the offspring. The mechanism functions in such a manner that half the offspring receive the substances in one proportion whilst the rest receive them in another, and so that either the male or the female substances are present in excess quantity. These substances act like enzymes—proportionally to their concentration. The quantitative difference of the substances in the two groups of individuals is automatically responsible for either the male or female enzyme completing the determining reaction first. This reaction is the production of specific hormones of sexual differentiation. How these hormones determine form-building is not yet clear, but it is probable that they are responsible for a difference in metabolism which in turn determines development of form.

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[1] Swingle, W., "Neoteny and the Sexual Problem." Amer. Nat., 55, 1920.—Witschi, E., 1921, "Development of Gonads and Transformation of Sex in the Frog." Amer. Nat., 55.

At this point the problem of sex touches the general determination problem, which receives most important advancement from the facts treated here. We see directly, for example, the chemical causes at work which induce a cell complex to grow into one form or another, to become symmetrical or asymmetrical, and in short to undergo all the differentiations which represent in their totality the diversity of the organization.[1]

But if we believe that we can foresee the solution of the fundamental problem of sex, this does not mean that we already understand all the details. We have left numerous individual problems on one side in the preceding pages and intentionally, in order not to confuse the main line of thought. In the following sections it will be our duty to fit these odd and special cases into the general scheme.

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[1] Further details in Goldschmidt, R., "Die Quantitativen Grundlagen von Vererbung und Artbildung."—Roux's "Votr. Abh. Entwicklungsmech," Heft 24, 1920.

SECTION III.—SPECIAL PROBLEMS AND ADDITIONAL FACTS

Amongst those questions bound up with the general problem of sex, the discussion of which will occupy the following pages, the first and most closely connected with the phenomena already treated is the problem of the inheritance of the secondary sexual characters. Many of the details have already been noted; we must now regard the subject as a whole.

CHAPTER IV

THE INHERITANCE OF THE SECONDARY SEXUAL CHARACTERS

IT is necessary first to be quite clear in regard to the significance of the problem. Let us recall for a moment the facts of sex-linked inheritance. Our study of this involved us in the consideration of certain characters which were inherited in a definite relation to the sex. Further analysis showed that the phenomenon indicated the presence of an ordinary Mendelian factor which, owing to its location in the X chromosome, was dragged into the mechanism of sex distribution. It had really as little to do with the sex as a passenger in a train is concerned with the steam pressure of the locomotive.

Now let us compare this with the secondary sexual characters. A study of the details of intersexuality has shown us that every individual is capable of developing the characters of either sex. What actually does develop is determined exclusively by the action of hormones of definitive form which are localized (Vertebrates) or non-localized (Insects). The heredity basis is identical in both sexes, but certain processes of differentiation and growth are of such a nature that they can be swayed in one direction or another through the action of specific hormones. There is nothing peculiar in this, it is a fact which holds good for every morphogenetic process. Thus we know that the absence of the thyroid gland hormone can result in a misbuilt dwarfed cretin who is certainly no less different quantitatively from the Venus de Milo than are the two sexes in many cases. We also know that the bees, by means of chemical changes in the food (changes which may also be regarded as hormonic), are able to obtain workers or queens with all their associated and physiological differences from the same kind of larvæ.

If, however, we may say that theoretically every morphological or physiological character of an animal can be differentiated under the influence of sex hormones into either the male or female type, this does not imply the existence of a corresponding number of secondary sexual characters whose heredity is to be studied, but that the characters inherited can react in two different ways with the two kinds of hormones. Accordingly a secondary sexual character is a character like all other hereditary characters which, however, in its morpho- or physio-genesis can be differently influenced by the specific male and female hormones (a conception always emphasized by Tandler, l.c.).

It follows from the above that there is no real problem of the inheritance of secondary sexual characters at all so far as normal sex dimorphism is concerned. Their identical basis consists in the totality of the inherited characters, their divergence is the product of specific hormone reaction. There is only a problem of inheritance in the matter of the hormone production, and the solution of this has been made known in the preceding chapters.

Naturally there are certain problems of heredity associated with these somatic characters which are so constituted that they can react to the sex hormones (and which are therefore distinguished as secondary sexual characters). In these cases it is a matter of distinguishing between the question of how the character concerned is inherited and the question of how the final result works out after the hormone action.

Problems of this kind are presented to us when forms with different secondary sexual characters are crossed, or when mutations occur in some sexually dimorphic form and are only visible when one of the two hormone reactions occurs—that is to say, when we have unisexual polymorphism, i.e. polymorphism limited to one sex only. We shall have to deal with such cases in the following pages. The simplest cases are again those where the reproductive organs do not possess the function of internal secretion—in the insects, for example. The cases of normal heredity may be considered first, and then the phenomenon of gynandromorphism which forms an important supplement to these.

(A) CASES OF NORMAL INHERITANCE

I. Forms without Internal Secretions from the Gonads

This group is subdivided into two externally different but internally closely linked subsections, the first comprising crosses between forms with different sex characters, and the second the phenomena of unisexual polymorphism.

a. Inheritance in Crosses, in which the Parents Differ in Regard to Secondary Sexual Characters

The preceding remarks on the nature of the secondary sexual characters lead us to expect that, when animals are crossed which differ in regard to these characters, some form of Mendelian inheritance will be found, differing from the ordinary cases in that the Mendelian combinations will only be visible in one sex; they will be sex controlled. Several experimental crosses of this kind are known. It is possible, for example, to undertake one with the Gipsy moth races, which were referred to earlier in the work when discussing zygotic intersexuality. The males of the Hokkaido, Schneidemuhl, and Aomori races are very clearly distinguished by the most evident secondary sexual character, the colour of the wings. The colour of the first named is very light, the Schneidemuhl males are more grey-brown in colour, whilst the Aomori males are deep black-brown (Fig. 74). Crosses show that these characters are inherited on Mendelian lines—naturally of course only within the male sex. But the females inherit the character concerned exactly as do the males; they simply cannot show it because the female hormones do not allow any wing colour at all to

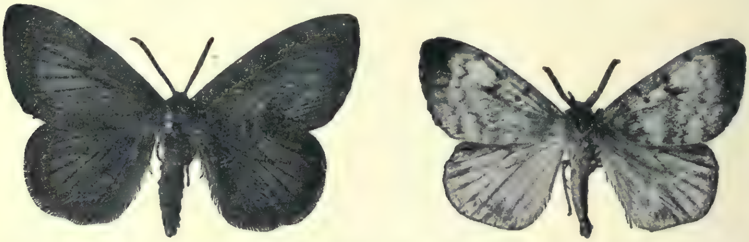

FIG. 74.—Males of the Aomori (left side) and Hokkaido races of *Lymantria dispar*.

appear. The accuracy of this view can be demonstrated when, by a suitable cross, the females become intersexual. In such a case they display exactly the wing colour typical of their brothers. And if any segregation so far as wing colour is concerned takes place among the males, the same kind of segregation may be found amongst the intersexual females, their sisters.

In the same manner it may be shown that a simple Mendelian segregation occurs when the females differ in such a character, even if both sexes are different. An example of such a cross is that between the different Japanese Gipsy moth races, the females of which possess yellow anal hairs, and the German forms with black-brown hair covering. The F_1 females present the character in an intermediate colour, but segregation takes place in the F_2 generation, and three types of females occur. Intersexual males conduct themselves exactly like the females so far as this character is concerned.

The investigations of Foot and Strobell[1] on the bug *Euschistus* may be brought forward as analogous. In the species *E. variolarius* the male possesses a black spot on the posterior end, the female is without it. The species *E. servus* has no spot on either sex. The F_1 generation of the cross gives males with a black spot, females without. In the F_2 generation, however, the females are again all spotless, but there are various types of males. Some have the black spot, others are without it, others again present all kinds of intermediate conditions. This experiment shows that the spot is a character whose differentiation is controlled by the male hormones and consequently it never appears in the female. In addition, however, its occurrence is determined by the presence of one or more Mendelian factors which are found in the species *E. variolarius*, but are absent from *E. servus*. These factors exhibit the ordinary Mendelian segregation and the numerical conditions indicate that we have a purely Mendelian problem of inheritance which concerns us no further here. These examples show clearly that the expectations which we have deduced and cited above are fulfilled.

It must be pointed out that these cases do not theoretically represent the only possibility—the only way in which secondary sexual characters may behave in inheritance. We have seen that their appearance indicates a reaction between a factorial complex which is present and a typical hormone or hormones. It might be possible, one would think, that the hormones concerned could be different in the races employed in the crosses, and so whilst the factors remained the same, different reactions could still result. Crosses would then give different results from those just described. Up to date, however, no case of this kind has been found.

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[1] Foot, K., and Strobell, E. C., "Results of Crossing *Euschistus variolarius* and *Euschistus servus*," etc. Journ. Linn. Soc., 32, 1914. The authors have altogether misunderstood the results of their investigation.

Still another possibility suggests itself, namely, that a sexual dimorphism might not be sex controlled at all, but brought about merely by some form of sex-linked inheritance. A very beautiful case has been recorded by Morgan,[1] and it will be very instructive to compare it with the foregoing, to make matters quite clear.

One of the mutations of eye colour in *Drosophila* is called eosin by Morgan. The results of crosses show (compare the previous discussions in regard to white eyes) that the factor for eosin lies in the X chromosome. Then the eosin females have two doses of the factor, one in each X chromosome, whilst the heterozygotic male has only one.. The eyes of the female are, however, always darker than those of the male since, as is elsewhere the case, the double factor doses give a deeper tone than single factor doses. This dimorphism has therefore nothing at all to do with the sex itself, but is a consequence, firstly, of the quantitative conditions of the factor and, secondly, of its position in the X chromosome.

Finally, reference must be made to still another possibility. The X chromosome as is well-known has frequently a partner (the Y chromosome) in the heterozygotic sex. (See *Drosophila*, p. 61.) In the usual experiments with sex-linked inheritance no hereditary factors appear to be met with in this Y chromosome. Now the author has been able to show[2] that in *Lymantria dispar* where the female is the heterozygotic sex, the female factor F apparently lies in the Y chromosome, an assumption which has since been confirmed.[3] Still more recently J. Schmidt and Aida[4] have shown that in fish, the male sex being heterozygotic, there are also certain factors in the Y chromosome, and in Schmidt's case these were the factors for secondary sexual characters which in crossing were purely paternal in inheritance. Thus when regarding cases of the inheritance of sexual characters which present difficulties of explanation, one must in future be prepared for the possibility of inheritance in the Y chromosome.

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[1] Morgan, Th., "Heredity and Sex." New York, 1913.

[2] Goldschmidt, R., "Intersexuality and Sex Determination." Biol. Centralbl., 39, 1919.

[3] Goldschmidt, R., "Untersuchungen Über Intersexualitat." Ztschr. ind. Abst., 23, 1920.—*Ibid.*, "Über Vererbung in Y Chromosome." Biol. Centralbl., 1923.

[4] Schmidt, Johs., "Racial Investigations, IV. The Genetic Behaviour of a Secondary Sexual Character." C.R. Laboratory, Corlsberg, 14, 8, 1920.—Aida, T.,

β. *Unisexual Polymorphism*

Unisexual polymorphism is the term applied when, as in certain species, chiefly butterflies, one sex occurs in one form only, but there are several quite different forms of the other. Thus to one form of the male swallow-tail butterfly there are several very different female forms. The principle of this phenomenon, which, on account of its close relationship to mimicry, has always aroused particular interest, can be regarded as explained. It is a case of a sex-controlled variety of local and geographical polymorphism. A few words concerning the latter may therefore be useful.

Geographical variability is the phenomenon of one and the same species presenting itself in different forms in different regions of its distribution area. Local polymorphism is the name given to the occurrence together of a more or less great number of typical varieties of a species in one and the same locality and at the same time. Geographical polymorphism is the term applied to the conditions when both of these phenomena are combined, and typical but different polymorphism is observed at different localities. The conditions are well known in Molluscs like *Helix*, *Achatinella*, and *Amphidromus*[1] and also amongst insects, particularly butterflies. An example from our own experience will make the matter clear.

In so far as geographical variability is concerned, the different variations, if inheritable, are really a question of a simple difference in the Mendelian factors. Thus the North European

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"On the Inheritance of Colour in a Fresh-Water Fish *Aplocheilus Latipes*, Temmick and Schlegel, with Special Reference to Sex Linked Inheritance." Genetics, 6, 1921.

[1] Coutagne, G., "Recherches sur le polymorphisme des mollusques de France." Ann. Soc. Agr. Sc. t. Ind. Lyon, 1885.—Lang, A., "Über die Mendelschen Gesetze." Schweiz. Naturf. Ges., 1905.—Gulick, J. Th., "Evolution, Racial and Habitudinal." Carn. Inst. Publ., 25, 1905.

Callimorpha dominula possesses a reddish ground colour in the wings, the Italian is yellow, and the difference is due to a Mendelian factor.[1] In crosses the F_1 generation is somewhat intermediate, orange, whilst the F_2 generation segregates typically in the proportion 1 : 2 : 1. Now the same species presents a very beautiful example of local polymorphism, and in a certain region of the Apennines an abundance of forms flying together differ amongst themselves in the degree to which the yellow coloration is displaced by black. All these forms reproduce promiscuously, and out of a single batch of eggs several of the variations may appear.

If these forms are crossed with the red-winged North European forms a segregation occurs in regard to the types of darkening (the invasion of black) in addition to that of the red and yellow colours.[2] This indicates that the local polymorphism concerned rests on a recombination of Mendelian factors for darkening.

It will be remembered that in the crosses of the different races of the Gipsy moth the distinguishing feature is a secondary sexual character of the male, the wing colour. Now if all these races were to be found at one spot instead of being distributed over Europe and Japan, and if free crossing took place between them, we should have unisexual polymorphism—one type of female with several kinds of males. The implication is, therefore, that this phenomenon means nothing more than the simultaneous presence of several distinct mutations differing in Mendelian factors which after crossing combine and recombine exactly as in local polymorphism. But there is a distinct difference from the latter, in that these factors belong to that group of characters which only reacts with the male hormones and consequently never can become visible in the female. Breeding results already carried out support completely this conception.

The best-known cases are the following: The American clouded sulphur (*Colias philodice*) presents one male form but two kinds of females, the one with white and the other with yellow wing ground colour. Gerould[3] was able to show that both these types gave a simple Mendelian segregation. The same segregation must also take place in the male, but it is not visible. A comparatively complete analysis of such a case was recently possible (Goldschmidt and Fischer).[1] The example was the fritillary *Argynnis paphia* and its second female form Valesina. In this case also the two females differ in a Mendelian factor whose action is invisible in the male sex. The same thing has been demonstrated by de Meijere-Jacobsen[2] for the swallowtail *Papilio memnon* and its three female forms Achates, Agenor, and Laomedon. But the most detailed analysis has been supplied by Fryer[3] working on the Ceylon species *Papilio polytes.* Fryer's work has established the fact that the earlier explanation put forward by de Meijere, Gerould, and the author[4] (and not given here) was incorrect, and it has led to the simple interpretation first put forward by Baur.[5] It fits in exactly with the deductions given above and solves the problem in principle.

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[1] In reality, probably two coupled factors, which comes to the same thing from the point of view of the mechanism of heredity.

[2] Our unpublished investigations.

[3] Gerould, J. H., "The Inheritance of Polymorphism and Sex in *Colias Philodice*." Amer. Natur., 45, 1911.

Papilio polytes possesses three kinds of females, one of which is like the male (female *cyrus*), whilst the other two (*polytes* and *romulus*) are quite different from it (Fig. 75). By breeding the progeny of these females and the different combinations which can be obtained from them, Fryer found that the males were always the same but that the females appeared in one, two, or all three forms according to the direction of the cross, and the numbers were in the proportions corresponding to a simple Mendelian segregation.

All the experiments could be explained on the following assumptions. When a dominant factor A is present in addition to the normal factorial constitution of the species, the *cyrus* colour character of the female is transformed into the *polytes* coloration. The factor is sex controlled, and therefore does not become visible in a male which bears it, but he can transmit

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[1] Goldschmidt, R., und Fischer, E., "*Argynnis Paphiavalesina*, ein Fall geschlechtontrollierter Vererbung." Genetica, 1922.

[2] De Meijere, J. C. H., "Über Jacobsens Zuchtungsversuche usw." Ztschr. ind. Abst., 3, 1910.—"Über Getrennte Vererbung der Geschlechter." Arch. Rass. Gesellschaftsbiol., 8, 1911.

[3] Fryer, J. C. J., "An Investigation by Pedigree Breeding into the Polymorphism of *Papilio Polytes*, Linn." Phil. Trans. R. Soc., 204, 1913.

[4] Punnett, R. C., "Mimicry in Butterflies." Cambridge, 1915.—Goldschmidt, R., "Bemerkungen zur Vererbung des Geschlechtspolymorphismus." Ztschr. ind. Abst., 8, 1912.

[5] Baur, R., "Einführung in die experimentelle Vererbungslehre," 2 Aufl., 1914.

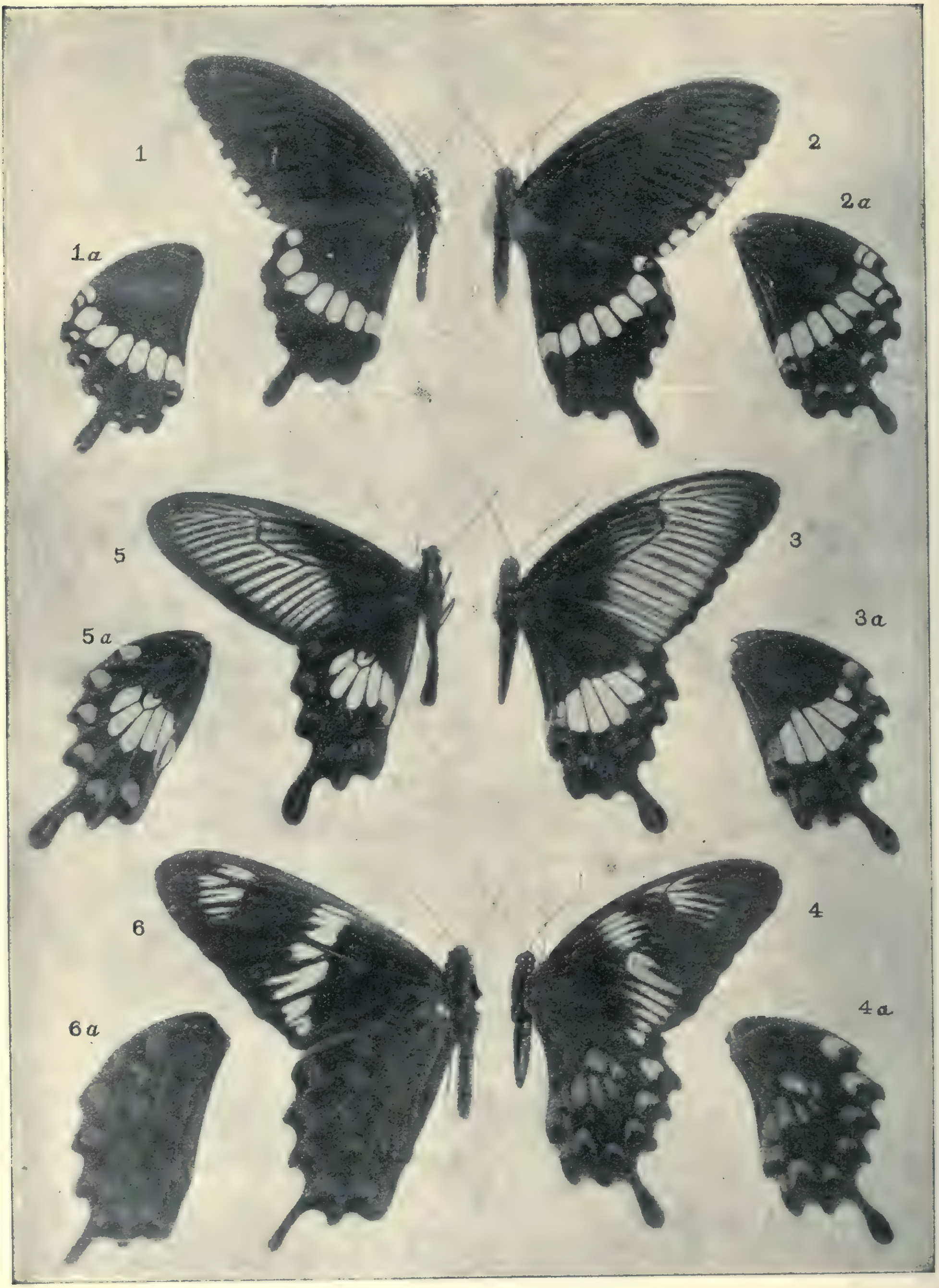

Fig. 75.—Polymorphism and mimicry of *Papilio polytes*.

1, ♂ polytes; 2, ♀ cyrus form; 3, ♀ polytes form, "mimic" of *P. aristolochiæ* (5 in figure); 4, ♀ romulus form, "mimic" of *P. hector* (6 in figure).

1a-6a, the underside of the posterior wings of the same specimens.

(It should be noted that the black-and-white reproduction of the coloured original is very imperfect.)

After Punnett.

to his daughters. There is also a second mutation B of such a nature, that, alone, the factor is without any visible influence and the *cyrus* form results, but in conjunction with A the *romulus* female is produced. On these lines the factorial constitution of the different forms possible is ;—

♂♂'s	*Cyrus* ♀	*Polytes* ♀	*Romulus* ♀
AABB	aabb	Aabb	AABB
AABb	aaBb	AAbb	AaBB
AAbb	aaBB		AABb
AaBB			AaBb
AaBb			
Aabb			
aaBB			
aaBb			
aabb			

Anyone acquainted with the elements of Mendelian inheritance can deduce the results to be expected from the different combinations, and Fryer found that the actual breeding experiments supported the theory. There is no need to go into further details, since the particular kind of Mendelian formula involved is not a matter which concerns our particular problem. The important point is to show that the phenomenon is of a Mendelian character.

This information permits of all analogous cases, even those of the greatest complication, being regarded as simple problems of Mendelian analysis. The African *Papilio dardanus* is a case in point. It is certain that this butterfly, with its numerous different female forms (*see* Fig. 76), several of which may occur in the same locality, is nothing but a combined case of local polymorphism, geographical polymorphism, and sex-controlled mutations. What this implies from the point of view of the theory of heredity follows from the above. As a matter of fact the phenomenon would scarcely have been regarded as of such great interest were it not at the same time bound up with mimicry, for apart from mimicry the same conditions can be demonstrated for quite common European species such as *Parasemia plantaginis.*

A word or two may be added, however, regarding this subject of mimicry. The fact is that in the case of *Papilio polytes*, as well as in *P. dardanus* and others, the different kinds of females resemble members of another group of *Papilio* altogether or even representatives of another family, which according to the well-known Bates-Müller-Wallace theories they are supposed to mimic. The female *polytes* "mimics" *Papilio aristolochiæ*, and the female *romulus* "mimics" *Papilio hector.* The biological side of the theory of mimicry does not concern us here, and we believe that Punnett has given the death-blow to the teaching of Wallace. There is a point, however, to which we would draw attention—one which is also of importance for the biological problem—and it is the following. The numerous known mutations of butterflies which depend on the presence or absence of a factor are variations of no great extent; yellow or red, yellow or white ground colour, partial darkening of the wings and such like, for example. In the mimicry cases referred to, however, we have alterations in which a difference of only one factor suffices to bring about extraordinary variations in appearance. Thus the females of *Papilio dardanus* are quite like members of another group of butterflies altogether—the Danaids (Fig. 76). It may be pointed out that it is just in these cases that we are concerned not merely with a simple factorial difference but a reaction of this with the hormones of female differentiation. Now it is exactly this sex hormone action that is able to direct the same substratum in two altogether different directions. Regarded only from the quantitative point of view the plumage of the male and female golden pheasant or the copulatory organs of male and female butterflies are as distinct from one another as any specific or generic differences. When, therefore, such a hormone reaction acting on substrata which differ factorially leads to extreme consequences, the result is not altogether surprising.

The cases of sexual polymorphism cited above all concern the female sex. From the point of view of principle there is no significance in this, and in the case of *Parasemia plantaginis* the corresponding forms are male. Theoretically an independent polymorphism of both sexes is also conceivable, but the writer is not certain whether a clear case of such a kind has been described. A sexual polymorphism of quite a different physiological significance will be met with in the section on hermaphroditism.

In concluding this section a word or two may be added on an interesting point. The "sex control" has, in the foregoing discussion, been understood as meaning that the hormones produced by the sex factors in one sex hindered the phænotypic appearance of the wing coloration concerned. Another explanation, however, is possible. The polymorphic sex was, in the cases analysed, the heterogametic sex (the female), and possessed an X-Y group of chromosomes. If now there was a pigmentation factor in the Y chromosome which reacted together with the autosomal factor in such a way that the coloration only appeared in the simultaneous presence of both factors, the result would be the same, i.e. the coloration would

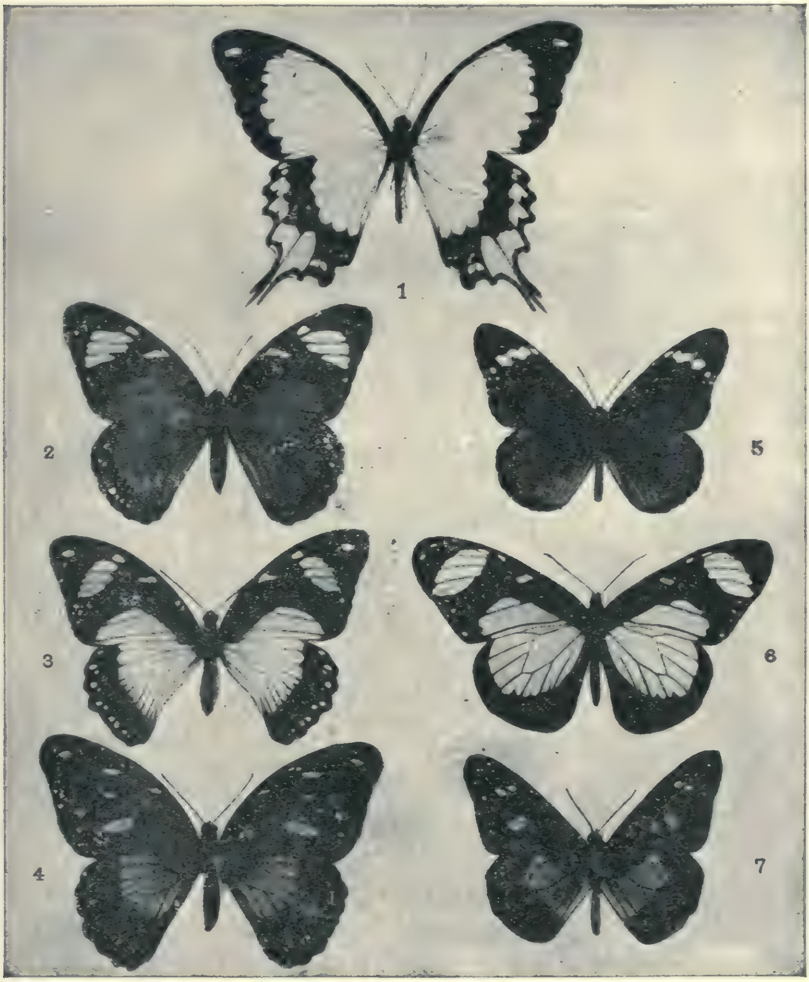

FIG. 76.—Polymorphism and mimicry of *Papilio dardanus*.

1, dardanus ♂; 2, ♀ trophonius form, mimicing 5, *Danais chrysippus*; 3, ♀ hippocoon form, supposed mimic of 6, *Amauris viavius*; 4, ♀ cenea form, "mimic" of 7, *Amauris echeria* (see remark below Fig. 75).

After Punnett.

only appear in the females since they alone possessed the Y chromosome

Evidence for the accuracy of this conception could be obtained if occasionally a factorial exchange occurred between the X and Y chromosomes. In such a case males of the particular form would be possible whose heredity could easily be deduced. In the *colias* form mentioned above white males are, as a matter of fact, occasionally observed (Gerould); their genetic analysis would be of decided interest.

2. The Inheritance of Secondary Sexual Characters in Forms with Internal Secretion of the Reproductive Organs

If we set out from our earlier considerations regarding the internal secretions and bring them into relation with the general discussion which introduced this chapter, there is at first sight no cause for assuming that the results of heredity should be different when internal secretions are present than when there is no localized hormone production. Further consideration, however, shows that the possibilities are at hand for greater complications. They present themselves most clearly in the best-known case of this kind, the inheritance of horns in sheep. Darwin was already acquainted with the fact that when Suffolks (hornless in both sexes) were crossed with Dorsets (horned in both sexes) the F_1 hybrid generation consisted of hornless females and horned males. Wood[1] has followed up the subject more exactly, and has shown that in the F_2 generation of this cross segregation takes place, giving—

Hornless ,	Horned ♀,	Hornless ♂,	Horned ♂.
3	1	1	3

Bateson[2] explains the result by assuming that the hornless race lacks a factor for horns which is present in the horned race, and this applies to both sexes. The presence of horns is, however, to be taken as recessive in the female and dominant in the male. Such being the case, if we denote the horn factor by H and its absence by h, all the HH animals will be horned and all the hh animals hornless. Amongst the hH animals, however, the males will be horned and the females hornless. The situation may be expressed in another way (as Morgan has done) and we can say that in the male one dose of H suffices to bring out the horn character whereas two doses are necessary in the female.

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[1] Wood, T. B., "Note on the Inheritance of Horns and Face Colour in Sheep." Journ. Agr. Sc., 1906.

[2] Bateson, W., "Mendelism." London, 1909.

The explanation fits in quite naturally with the facts, as is shown by the following scheme where the dominant character is printed in heavy black :—

	Suffolk ♀	×	Dorset ♂
	hh		**HH**
F_1	hH		h**H**
	female without horns		male with horns
F_2	$\underbrace{\mathbf{HH} + 2hH + hh}$		$\underbrace{\mathbf{HH} + 2h\mathbf{H} + hh}$
	1 horned ♀ 3 hornless ♀		3 horned ♂ 1 hornless ♂

Now it is clear that this formula gives no real explanation, and the same is equally true of others since put forward by Arkell and Davenport, the author,[1] and others. They are all only symbolic paraphrases in which other attributes, such as sex-limited change of dominance or inhibition factors, are added to the well-known Mendelian mechanism of segregation and are supposed to mitigate the obscurity. A real explanation necessitates the most exact knowledge of the relation of the internal secretions to the character for horns. Is it a fact that the Suffolk race really has no factor for horns? What happens when castration is performed on both sexes, or when heterologous gonads are transplanted from the same or from a horned race? How do the Dorsets respond to the same experiments, and what is the position in regard to the six types of F_2 hybrids? Until these questions are answered a satisfactory solution is not to be expected.

Now the following facts are further known: In races of sheep where both sexes are equally well horned castration has no effect on the development of horns (the same thing applies in the analogous case of the reindeer. See Tandler). In races, however, where the males have better developed horns than the females, the growth of such horns is hindered by castration. Where the males possess horns but the females are hornless, as is the case with Merinos, the effect of castration on the males is complete loss of horns (Castle[1]). The possibility is thus present that in addition to differences in the factorial constitution of the races we may have differences in the quality of hormone action. And yet a further possibility of complication is given which may be deduced from Morgan's investigations on the Sebright bantams.[2] It has been already described how in this race the cocks have hen plumage. Morgan and Punnett found that the castration of these cocks had the unexpected effect of bringing out the development of the male plumage (Fig. 77). Here the internal secretion of the male sexual glands has the singular effect of hindering the development of a male character.

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[1] Arkell and Davenport, "The Nature of the Inheritance of Horns in Sheep." Science, 35, 1912.—Goldschmidt, R., "Einführung in die Vererbungswissenschaft," 2 Aufl., 1913.

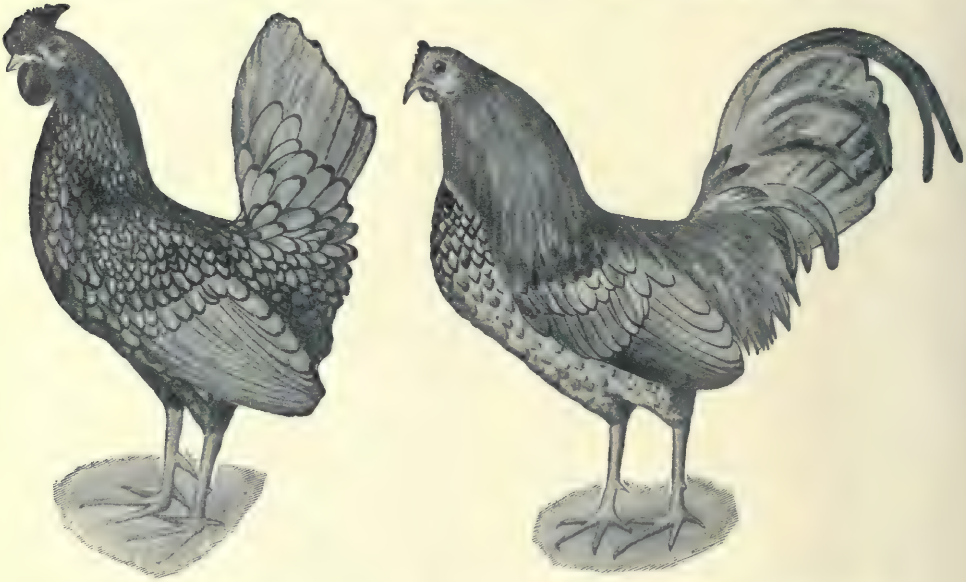

Fig. 77.—Sebright bantam. On the left normal cock with hen plumage. On the right, the same bird after castration (note male plumage). After Morgan.

When these hen-feathered Sebrights were crossed with normal races a simple Mendelian phenomenon was observed and segregation occurred in the F_2 generation so far as the hen feathering was concerned. It is clear, therefore, that a Mendelian factor is present which determines the perverse hormone reaction.

[1] Castle, W. E., "Horns in Sheep a Sex-Limited Character." Science, 35, 1912.

[2] Morgan, Th. H., "Demonstration of the Appearance," etc. Proc. Soc. Exp. Biol. Med., 13, 1915.

It will be seen that this chapter is not yet ripe for discussion. Its complete elucidation may well be of the greatest importance in regard to the physiology of heredity.

B. GYNANDROMORPHISM

Teratology plays an important rôle in experimental biology and with justification, for abnormalities always teach us something of the possibilities of certain processes, and their analysis may throw important light on normal events.

For this reason sexual abnormalities occasionally found in nature have aroused justifiable interest and played an important part in the theoretical discussions. In particular we refer here to the mosaic hermaphrodites usually occurring in the form of bilateral hermaphrodites, the two halves of the body being different in sex. For these cases we should like to see the term gynandromorph reserved — a name often employed for intersexual individuals. The essential feature of gynandromorphism is the presence in an individual of one sex, of sharply marked off parts of the body which bear the characters distinctive of the other sex. Generally, as noted above, such a gynandromorph has one half of the body, including the reproductive organs, male whilst the other half is female. There are, however, also cases in which the gynandromorphism is anterior-posterior in type and, although more rare, other cases still in which every possible kind of sex mosaic occurs. These mosaic formations are not limited to the sexual characters alone. They are found occasionally in hybrids, only the somatic character, being concerned. An interesting case of this kind which Dr. Seiler found in our Gipsy moth cultures is illustrated in Fig. 78. Here, a caterpillar which is a hybrid between the Hokkaido and Fiume races presents the pure characters of the Fiume race in the right posterior quarter of the body, whilst the rest of the animal is hybrid in appearance. A normal female arose, however, from the pupa. An explanation of this phenomenon, so called somatic segregation, is not difficult if

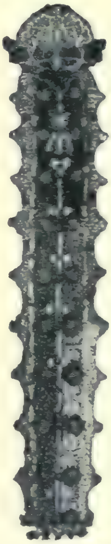

FIG. 78. — Hybrid caterpillar of *L. dispar* with somatic segregation.

one assumes that definite abnormalities in the chromosome distribution take place during development. And it is on this principle that the present-day explanation of gynandromorphism depends.

It will be advantageous to begin with the more simple conditions as met with in the group Insecta. A group of typical insect gynandromorphs are depicted in Fig. 79—they belong to different families and all are of the bilateral type.

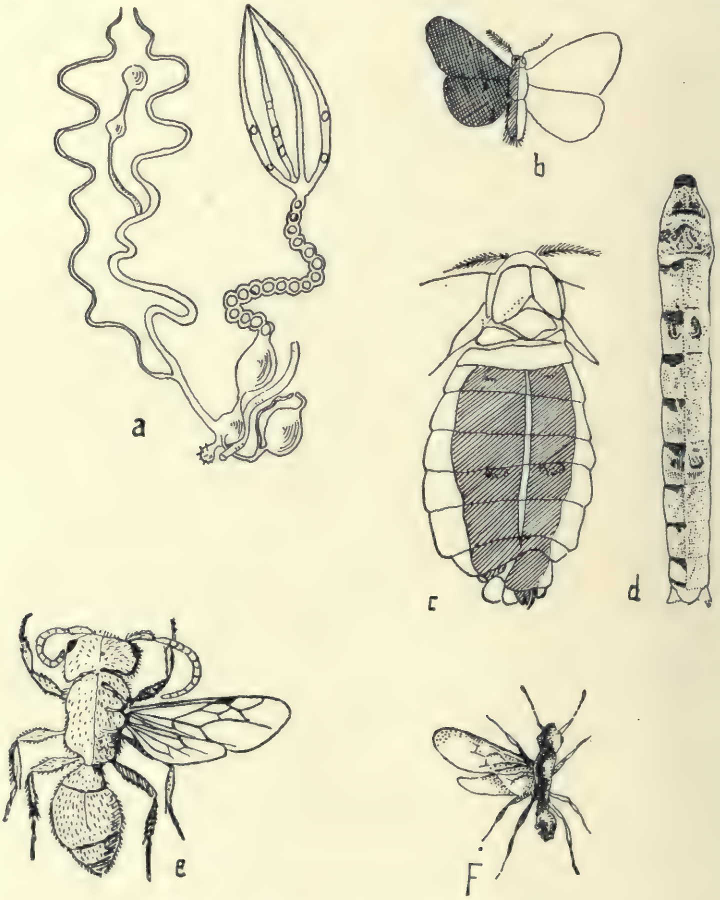

FIG. 79.—Types of gynandromorphic insects.

a, Reproductive apparatus of a bilateral gynandromorph of *Gastropacha quercifolia* (male on left side, female on right); b, the winged insect from which the above was taken. After Wenke. c, body of a similar kind of gynandromorph of a silkworm which came from the hybrid caterpillar d (the latter presents the parents' characters separated). After Toyama. e, gynandromorph of the wasp *Pseudomethoca canadensis*. From Morgan; f, gynandromorphic ant, *Myrmica scabrinois*.

The most obvious explanation of these gynandromorphs is the assumption of some abnormality at or after fertilization, which results in the segmentation nucleus for one symmetrical half of the body coming to possess one X chromosome whilst the other nucleus possesses two. Keeping in mind the type of determination already made clear in the insect group, this would naturally give bilateral hermaphroditism as depicted. As to the way in which such an abnormal chromosome constitution could arise, a little light is thrown by the gynandromorphs which are hybrids between different races and where the different characters of parts of the body correspond to the differences in racial characters of the parents. An example is the silk worm gynandromorph (Fig. 79 d). It is evident in this case that the whole nucleus must have taken part in the abnormal division and not merely the sex chromosomes.

A more exact analysis has been possible in the case of the remarkable bee gynandromorphs owing to the relationship between parthenogenesis and sex (to be discussed later). It is general knowledge that parthenogenetic eggs of the bee give rise to drones (males), whilst fertilized eggs develop into workers and queens (females). Now Boveri[1] observed that under certain abnormal conditions the nucleus of the spermatozoon which had penetrated a sea urchin egg came to rest in a kind of paralysed condition, whilst the centrosome pressed on to the egg nucleus and set the karyokinetic division going. The sperm nucleus then came to lie merely according to chance in the one or other cell resulting from the first division, to the nucleus of which it could unite. Two blastomeres thus result, one containing only the maternal nucleus whilst the other possesses both male and female nuclear elements. If the same thing occurred in a bee's egg the cell descendants of the one blastomere would correspond to those of a fertilized egg, whilst those of the other would be like the descendants of a parthenogenetic egg and a gynandromorph would naturally result.

Another explanation identical in principle but different in details has been given by Morgan.[2] He assumes that the egg is normally fertilized, but that in addition a second spermatozoon penetrates it and takes part with its nucleus in the development. This possibility has also been realized in the sea urchin eggs and the observation can be utilized for purposes of explanation.

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[1] Boveri, Th., "Über partielle Befruchtung. Sitzber." Gesell. Morph. Phys. München, 4, 1888.

[2] Morgan, Th. H., "An Alternative Interpretation of Gynandromorphism in Insects." Science, N.L., 21, 1905.

Finally Doncaster[1] has drawn attention to a third possibility in connection with his discoveries on *Abraxas* eggs, namely, the fertilization of two egg nuclei, with or without X chromosomes. Naturally this explanation cannot be utilized for the bee gynandromorphs. The long famous case of gynandromorphism in bees is that of Eugster's hermaphrodite bees. Eugster possessed at Constance in the sixties of the nineteenth century a beehive with hybrids between an Italian queen and German drones. This stock produced regularly for some years a large number of gynandromorphs which were subjected to an exact investigation by v. Siebold.[2] When the Italian queen of the hive died Eugster obtained a hybrid queen which likewise produced gynandromorphs. These, however, were somewhat different from the earlier ones. Recently the original material has been again examined by Boveri and Mehling[3] and the following is the

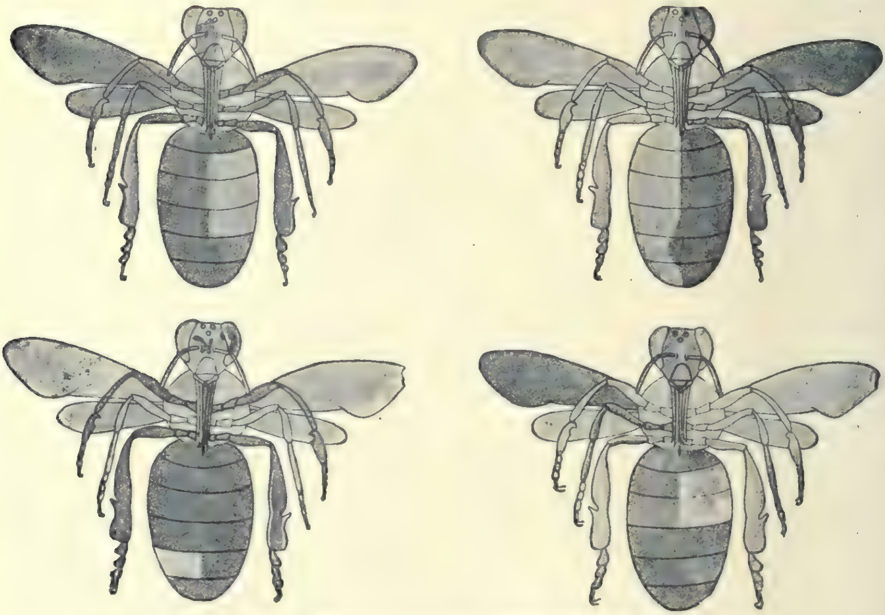

FIG. 80.—Diagram illustrating four of Eugster's bee gynandromorphs. Male parts light; female dark shading.

After Mehling.

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[1] Doncaster, L., "The Determination of Sex." Cambridge, 1914.

[2] v. Siebold, C. Th., "Über Zwitterbienen." Z. Wiss. Zool., 14, 1864.—Ders., "Bienenztg." 1866.

[3] Boveri, Th., "Über die Entstehung der Eugsterschen Zwitterbienen." Arch. Entwicklgmech., 41, 1915.—Mehling, E., "Über die gynandromorphen Bienen des Eugsterschen Stockes." Verh. Phys.-med. Ges. Würzburg, 43, 1915.

outcome. The mosaics which comprise all the sexually different organs of the body are of very different kinds. There are purely lateral hermaphrodites as well as anterior-posterior cases. In addition there are all sorts of other combinations down to the minimal interpolation of the organs of one sex into a body which otherwise is of the opposite sex. Fig. 80 is a schematic illustration of four such types, the male parts are denoted by light, the female by dark shading. In addition there are two figures of parts of the body. Fig. 81 depicts the heads of workers, drones and four different gynandromorphs; Fig. 82 illustrates the very characteristic hind legs of the workers and males compared with those of gynandromorphs.

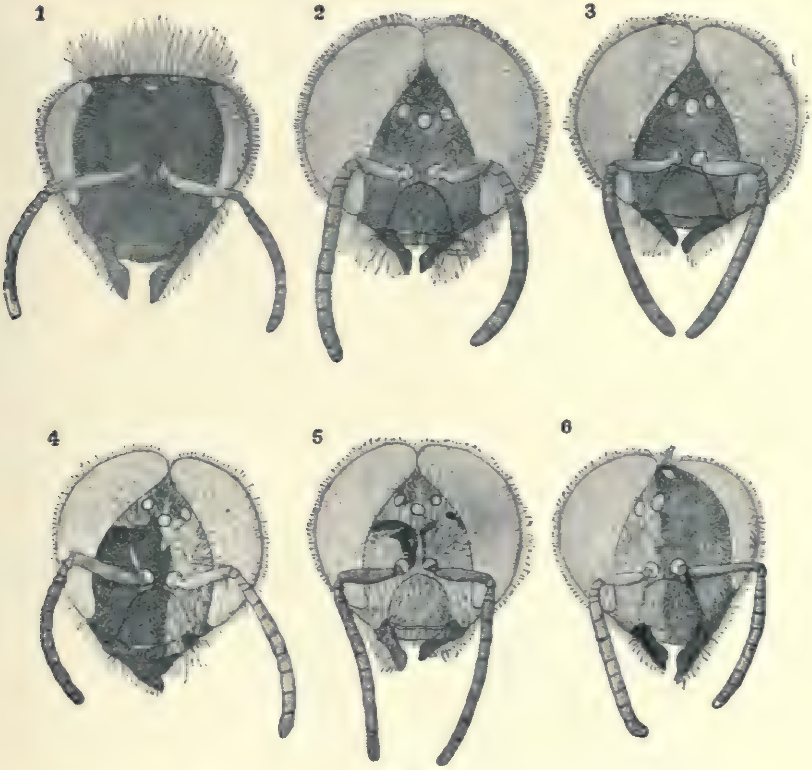

Fig. 81.

Upper row: heads of worker bee (1), drone bee (2), and drone (3). Lower row: heads from three different Eugster bee gynandromorphs.

After Mehling.

Now since the gynandromorphs in this case were hybrids of different races the possibility was forthcoming of deciding whether any given mosaic part possessed the hybrid character and was thus the descendant of fused germ nuclei or was purely paternal or maternal in character, hence possessing only egg nuclear or sperm nuclear material. Boveri found that all the male parts were typically Italian in character, whilst the female parts possessed the hybrid character. This of course shows that his hypothesis cited above is probably correct.

This does not mean, however, that every case of gynandromorphism must be explained exactly in this way. The irregularities in fertilization to which Morgan and Doncaster have referred are just as likely to lead to the origin of gynandromorphs in other cases. It is not even necessary that the disturbance of the X chromosome mechanism should take place at the time of fertilisation. Every embryonic cell division offers opportunity for abnormalities in the chromosome distribution which may give rise to gynandromorphism if it leads to the resulting cells having either only one or both X chromosomes. And according to the embryonic stage at which this takes place the gynandromorphs produced will be bilateral,

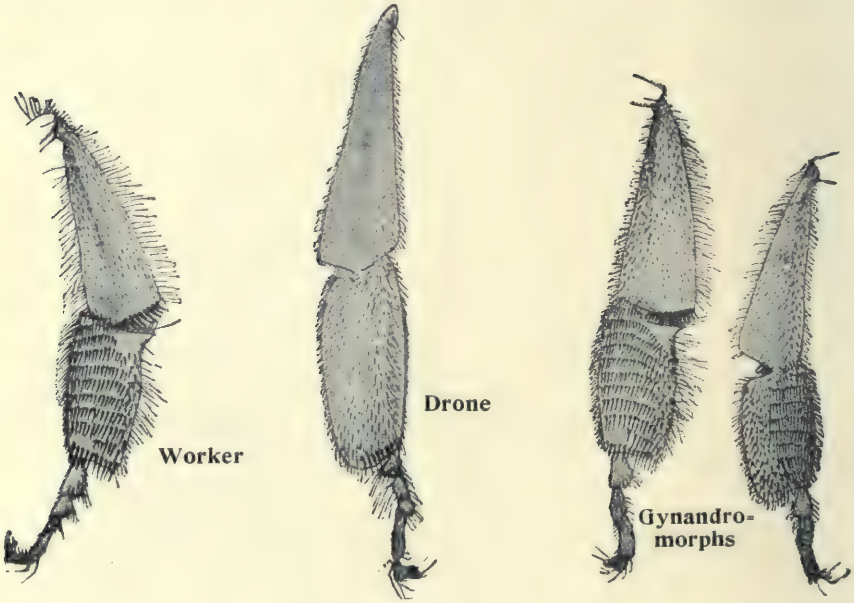

FIG. 82.

a, right hind leg of worker bee, inner side; b, the same leg from a drone; c, the same legs from one of Eugster's gynandromorphs.

After Mehling.

quartal, or some other kind of sex mosaic. In the investigation of that extremely favourable example, *Drosophila*, Morgan was able to obtain direct evidence of such processes.

The brilliant analysis of the gynandromorphic individuals of *Drosophila* carried out by Morgan and Bridges[1] was rendered possible by the previous thorough investigation of the mechanism of heredity in this fly—an analysis carried further, as is well known, than in any other animal. The inheritance of numerous somatic as well as sex-linked characters has been made out and analysed. If gynandromorphism occurs in individuals which are hybrids in several of these characters, the male and female parts of the hybrids will indicate, without anything further, the nature of the chromosome constitution. Now Morgan and Bridge's observations showed that the ordinary inherited somatic factors were not concerned in the phenomenon, whilst on the other hand the sex-linked factors were clearly involved. It follows that the male and female mosaic parts differ from each other in the X chromosome constitution. If the dominant factor A for long wings and its recessive allelomorph a for short wings are located somewhere in the X chromosome, the hybrid female Aa will be long winged since it possesses two X chromosomes, one with A and one with a. When for any reason the X chromosome with A is missing from one-half of the body, that part will be male (male heterozygotism, one X = male) and also short winged. In the same way one can determine exactly the chromosome constitution of every mosaic part of a gynandromorph.

By following this plan it was demonstrated that the elimination of the X chromosome was the factor determining gynandromorphism. In some embryonic cell division one X chromosome through some abnormality in division becomes shut out from one of the daughter nuclei, so that one of the two daughter nuclei is of male and the other of female chromosome nature, and this feature is of course handed on to all the descendant nuclei. Naturally this conception implies that all gynandromorphs arising in this way must be genetically females (XX), and it is only when the elimination of the chromosome occurs at the first segmentation division that bilateral gynandromorphism results; in all other cases the individuals must be predominantly female with greater or less male invasion according to the stage of embryonic development at which the elimination took place. This is actually the case in *Drosophila.* Further interesting details need not be given here, since the above is sufficient to show that these gynandromorphs actually arise through elimination of X chromosomes. The whole case naturally furnishes an important link in our chain of evidence demonstrating the accuracy of the chromosome mechanism of sex distribution.

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[1] Morgan, Th. H., and Bridges, C. B., "The Origin of Gynandromorphs." Carnegie Instit., Washington. Publ. 278, 1919.

Morgan and Bridges are inclined to explain Eugster's bee gynandromorphs in a similar way. In principle it is all the same whether this is correct or whether Boveri's explanation remains upheld, for both run along the same general lines—they depend on an abnormality in the X chromosome mechanism.

All things considered therefore it has been shown that gynandromorphism in insects is the consequence of a disturbance in the sex chromosome mechanism.

In the case of gynandromorphism in animals with internal secretions of the gonads the matter is not so simple. A number of real gynandromorphs of this kind, taking the form of bilateral hermaphrodites, are known amongst birds—the finch studied by Weber, a bullfinch described by Poll,[1] and a pheasant investigated by Bond. In the first two cases the right side of the body was male, the left female, in regard to the secondary characters as well as the reproductive organs. In Bond's pheasant the sides of the body were of the converse type, and the reproductive organs contained both male and female parts in one organ. In the last case there is also to be mentioned a very important fact from the point of view of the physiology of development—the individual tail feathers had one half the vane with male and the other with female marking (Fig. 83). At first sight one might think of Boveri's scheme for explaining the phenomenon. But then we are faced with the extraordinary difficulty of accounting for the action of the internal secretions. One can scarcely imagine them as separated in the two halves of the body. Without doubt there is a difficulty here which at present seems in no way surmountable. Reference may be made to our discussion in previous pages on hormonic intersexuality, in particular on the nature of hormone action in birds and mammals. Since the control of sexual differentiation in the birds is not yet completely in the hands of the glands of internal secretion, real gynandromorphism is quite conceivable. In mammals, however, it should no longer be possible. Whether any of the numerous described hermaphrodites and pseudohermaphrodites of mammals can be regarded as gynandromorphs it is impossible to say at present. In this connection reference may be made to the chapter on Hermaphroditism.

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[1] Poll, H., "Zur Lehre von den sekundären Geschlechtscharakteren." Sitzber. Gesellsch. naturf. Fr., Berlin, 1909.—Bond, C. I., "On a Case of Unilateral Development," etc. Journ. Genetics, 3, 1913-14.

Finally, attention must be paid to a particularly interesting point, namely, that real gynandromorphism also occurs as an hereditary character. Eugster's bees indicated this, since one particular queen regularly produced gynandromorphs. We know of cases, however, in which the same thing has been followed through several generations. Naturally it is very much to be desired that a case of this kind should be analysed genetically; it should be possible since cases of inherited gynandromorphism have also been observed amongst insects by breeders. Probably one could find out by hybridization experiments what it is that determines that in every generation a certain percentage of individuals (probably of only one sex) should present abnormalities in the chromosome mechanism; a case of this kind has already been undertaken by the author.

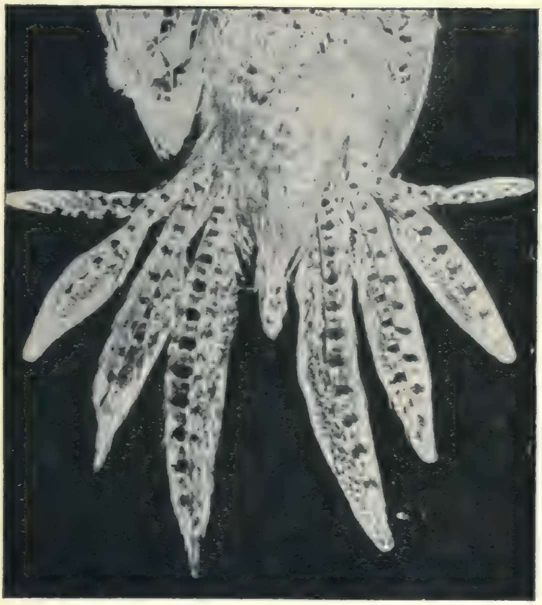

FIG. 83.—Tail feathers of a hermaphrodite pheasant with bilateral male coloration.

After Bond.

In conclusion, emphasis may once more be laid on the necessity for a sharp distinction between gynandromorphism and intersexuality. A gynandromorph is a sex mosaic in space in which male and female parts lie, from the point of view of the physiology of development, adjacent and equivalent to each other; they are present simultaneously during the course of development. An intersex is a sex mosaic in time, male and female parts may be found side by side, but from the point of view of development one part is younger than another; the result is that at a given time during development the whole individual is of one sex whilst at a later time it is of the other. Genotypically a gynandromorph is the product of a disturbance in the *mechanism* of sex distribution, an intersex is the product of a disturbance in the *physiology* of sex determination. Phænotypically a gynandromorph is a sexual mosaic, an intersex is an organism intermediate between the two normal sexes. The scheme (Fig. 84) should make the important difference between the two more clear. On the left is shown the development of two types of gynandromorphs; the dotted lines indicate the cell generations with the male chromosome nature, the continuous lines those of female nature. Both run adjacently to each other. On the right is the representation of the development of intersexes, the individual starts as female and then continues as male or the converse.

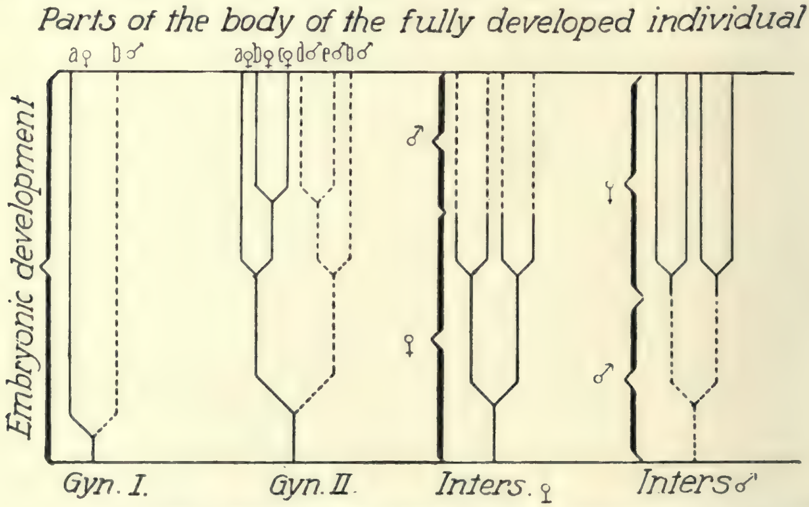

FIG. 84.—Diagram illustrating the difference between gynandromorphism and intersexuality (the dotted lines indicate male development, the continuous denote female development).

CHAPTER V

HERMAPHRODITISM

THE phenomenon of gynandromorphism has been and is often regarded also as hermaphroditism and considered under this head Since one must define hermaphroditism as the occurrence of individuals which produce both male and female germ cells in the same body it will be seen that there is some reason, at least in many cases, for classifying gynandromorphs under this head. That we have not done so has its *raison d'être* in the fact that genetically as well as physiologically the phenomenon of gynandromorphism has nothing to do with normal hermaphroditism and plays no part in the explanation of the latter. Gynandromorphism is rather a question of a teratological event that belongs to the same group as the chimæras in the plant world and the mosaic hybrids in the animal world. Gynandromorphism is associated in the closest manner with the normal phenomena of inheritance of sex and secondary sexual characters. Real hermaphroditism is something different. Here the genetic constitution of the whole body is such that normally both kinds of germ cells are produced in the one organism. It is clear that this introduces a new problem altogether, the solution of which to a certain extent is independent of the problem of bisexuality, although certain fundamental facts such as the physiological basis of sex differentiation must be identical.

Unfortunately we must understand at the outset that at present this is the most unsatisfactory chapter in the whole sex problem, and up to date our material is insufficient to permit of a correct genetic or physiological understanding. An accurate judgment of the facts at present known is, however, a necessity for further progress, and we shall seek to obtain this in the following.

If we regard all the cases in which the two kinds of germ cells are normally produced in the one organism as hermaphrodites, we shall have some very different types of hermaphroditism, the significance of which for the whole problem is very different. In the first place two large groups may be distinguished which we can denote briefly as functional and non-functional hermaphroditism. In the first the two kinds of germ cells produced are intended to function—that is to take part in fertilization. In the second group it is a question of really bisexual animals in which one or both sexes permanently or transitorily produce both kinds of germ cells—of which, however, only one kind is functional. This latter type is clearly a special case of bisexuality which on the one hand must be explained in terms of bisexuality, but which on the other hand can help us to understand functional hermaphroditism. It will be as well, therefore, to begin with non-functional hermaphroditism.

A. Non-functional Hermaphroditism

This group comprises several very remarkable complexes of phenomena of different physiological value which are of the greatest importance for the problem in its entirety. The most important of these have already been treated in our chapter on intersexuality, so that we need only add the less important individual occurrences here.

1. Accessory Hermaphroditism

The presence of a rudimentary ovary in male animals may be denoted as accessory hermaphroditism; the best-known case is that of the so-called Bidder's organ in toads. Its presence and its structure as a rudimentary organ have been long known. At the anterior end of the testis there is a spherical body with the structure of an ovary, although even in the fully developed condition the histological details are somewhat different from those of a functional ovary. Fig. 85 gives the position and structure of this remarkable body. It is found in both sexes when young, but it degenerates later on in the females and remains only in the males.[1] It is now known that in the course of the year this organ undergoes alterations parallel with the sexual cycle. In the summer, particularly when sperm formation is taking place, a regeneration occurs. Harms[1] was able to demonstrate experimentally that this organ possessed an internal secreting function. One of the secondary sex characters of the Amphibia which is dependent on the internal secretion of the testis is the development of the thumb pads. Now if either the testis or the organ of Bidder is extirpated no effect on the thumb pads results. If both, however, are removed the latter do not develop, but their development can be aroused if a Bidder's organ is transplanted and healed into the dorsal lymph sac. Thus the organ of Bidder is a rudimentary ovary which has suffered a change of function and become an organ of internal secretion. Consequently it is retained in the adult.

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[1] For further details see H. D. King, "The Structure and Development of Bidder's Organ in *Bufo lentiginosus*." Journ. Morph., 19, 1908.

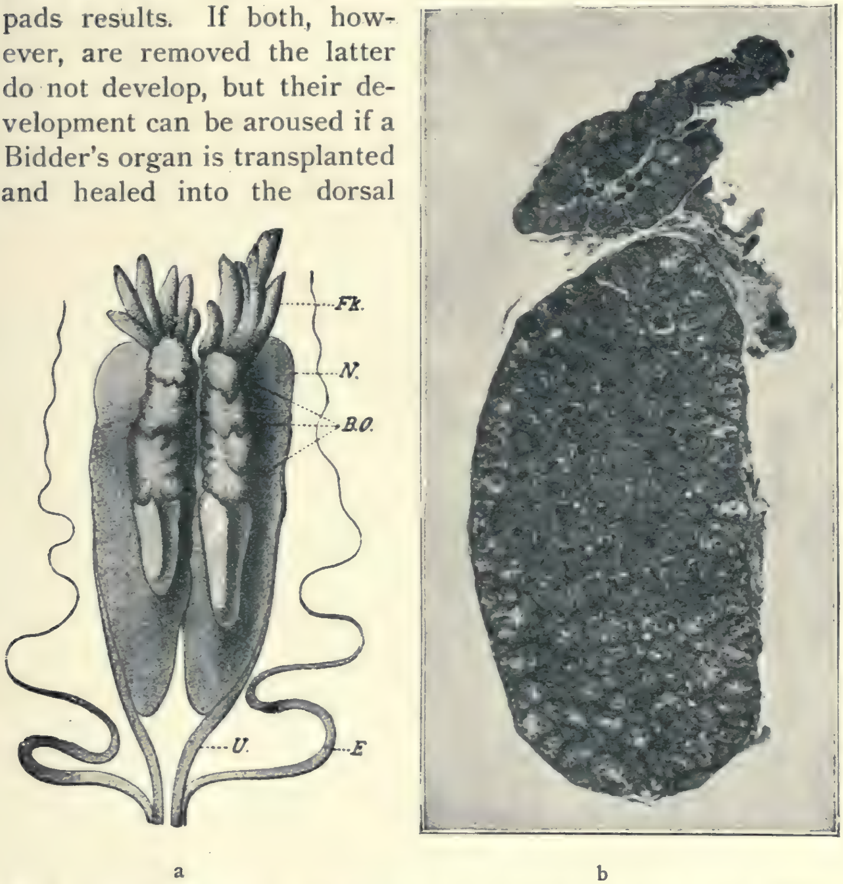

Fig. 85.—Organ of Bidder. a, general view of the testes and kidneys (after Knappe); b, section through testis and Bidder's organ.

BO, organ of Bidder; E, Mullerian ducts; U, Wolffian ducts; N, Kidney; Fk, fat body.

Preparation and Photo made by Prof. Poll.

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[1] Harms, W., "Experimentelle Untersuchungen Über die innere Sekretien der Keimdrüse." Jena, 1914.

And although it is only in the toads that it attains such a typical development, something quite similar is also occasionally found as an abnormality in other Amphibia—frogs and salamanders, for example.[1]

Cases which may be compared directly with this are very rare indeed. A very notable one is the accessory hermaphroditism of the Pseudoneuropteron—*Perla marginata.* All the males in this case possess a beautifully developed but nonfunctional ovary in front of the testis, as is illustrated in Fig. 86 (after Schönemund[2]). Regarding its function nothing is known.

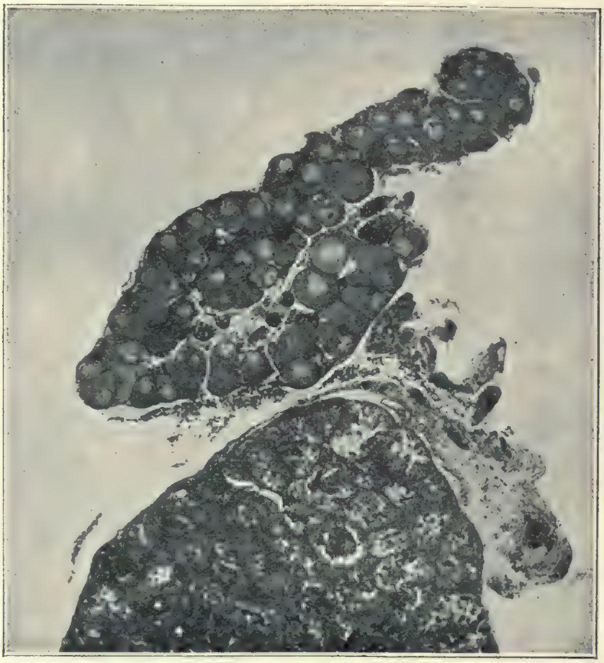

FIG. 85c.—Anterior portion of the organs shown in Fig. 85b, more highly magnified to show the ovarian structure of Bidder's organ.

Preparation and Photo by Prof. Poll.

These cases have naturally nothing directly to do with functional hermaphroditism. We believe rather that they are explainable through the earlier discussed conditions of transitory intersexuality in frogs. They would appear to be examples of embryonic intersexuality which, at least in the case of the organ of Bidder, has acquired in a sense a certain degree of permanence, the female parts of the gonad of the males having to a greater or lesser extent undergone a change of function into a gland of internal secretion. As such they have persisted, keeping in part the gonad structure.

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[1] Literature cited by H. D. King, "Some Anomalies in the Genital Organs of *Bufo lentiginosus.*" Amer. Journ. Anat., 10, 1910.

[2] Schönemund, E., "Zur Biologie und Morphologie einiger Perlaarten." Zool. Jahrb. An., 34, 1912.

In other comparable cases nothing is known of such a change of function, but the most probable assumption is that developmental conditions like those associated with transitory intersexuality in frogs are concerned which, however, are not followed by a subsequent elimination of the ovarial part of the testis. In principle then the case is of the same nature as the retention of the Müllerian ducts in many Amphibia or the parovaria, etc., in female mammals. In insects and Crustacea one finds as a matter of fact all the stages of such accessory hermaphroditism realized, and they provide material for such an explanation as the above—a preliminary explanation it is true so long as experiments fail.

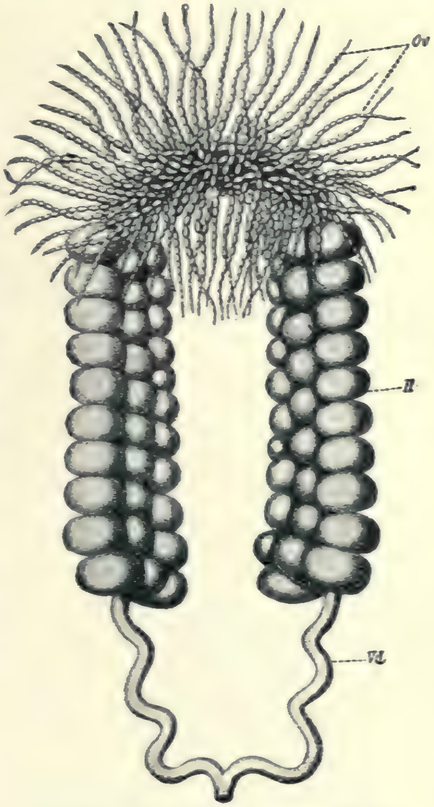

Fig. 86.—Reproductive organs of *Perla marginata*.
Ov, ovarian tubules; H, testis; Vd, vas deferens.
After Schönemund.

Heymons[1] was able to show that in *Blatta germanica* a part of the sex gland fundament of the male was normally differentiated to a small extent in the female direction. In many cases this goes so far that primitive oviducts are formed and egg cells begin to develop. Occasionally remains of the *anlage* are found up to the Imago stage (Isopods, Decapods). In *Orchestia*, again, according to Nebeski,[1] a part of the testis always contains eggs, and according to Ischikawa[2] the testes of *Gebia* are always differentiated into a posterior part, which is ovarial in nature containing eggs that cannot function, and an anterior testis section (Fig. 87); other occasional notes point to a wider distribution of these conditions. In the Crustacea the secondary sexual characters appear also to have been drawn into the phenomenon, for it is often stated (and anyone who has to deal with large numbers of crayfish in school courses can support this) that

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[1] Heymons, R., "Über die Hermaphrodite Anlage der Sexualdrüsen beim Männchen von *Phyllodromia germanica*." Zool. Anz., 13, 1890.

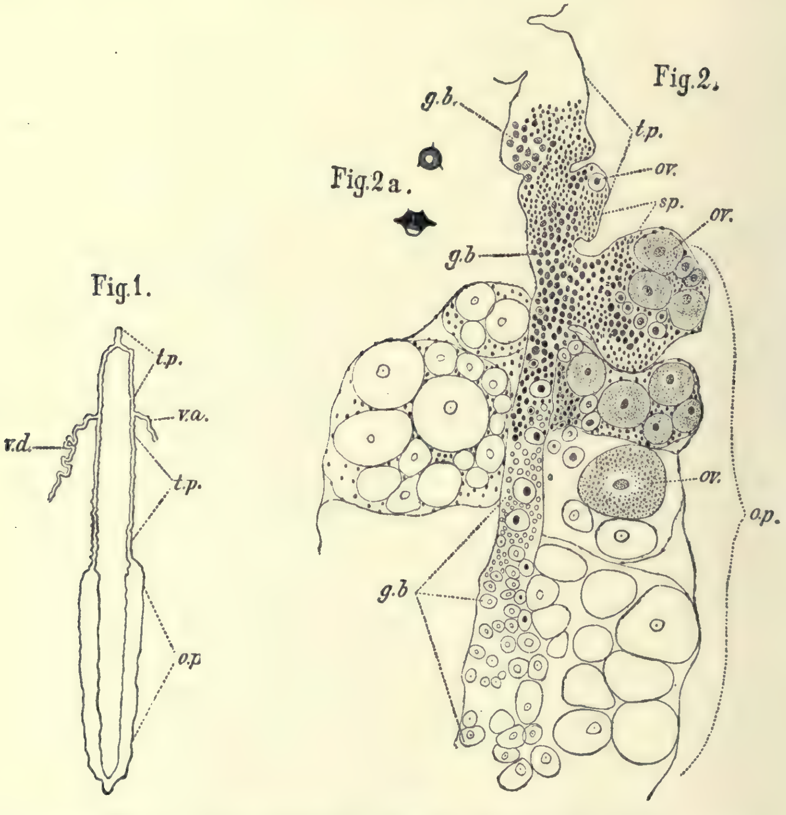

FIG. 87.—Male reproductive organs of the crab *Gebia major*.
1, testis from above; 2, longitudinal section at place of transition of ovarian and testicular portions; 2a, ripe spermatozoa.
gb, Keimbahn; op, ovarial part; ov, eggs; sp, sperms; tp, testis part; vd, vas deferens.
After Ischikawa.

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[1] Nebeski, "Beiträge zur Kenntnis der Amphipoden der Adria." Arb. Zool. Inst. Wien, 1880.

[2] Ischikawa, C., "On the Formation of Eggs in the Testis of *Gebia major* de Haan." Zool. Anz., 14, 1891.

in Decapods the males frequently possess the rudiments of female sex apertures and oviducts, whilst females possess more or less well-developed copulatory appendages.

The accuracy of the interpretation given here in regard to Bidders' organ follows very beautifully from an investigation recently carried out by Harms.[1] In about 10 per cent of the male toads examined he found between the organ of Bidder and the testis a transition zone with ovarial characters where ripe egg cells also developed. If such males were castrated their secondary sexual characters remained unchanged under the influence of the organ of Bidder, but the ovarial region began to grow and develop into a real ovary. Attention may be drawn to the resemblance between this condition and the adult frog hermaphrodites referred to previously.

Possibly the often-cited hermaphroditism of *Myxine* should be placed here, for Schreiner[2] has brought forward evidence that no real hermaphroditism occurs in this example. One finds rather all transitions from individuals with testes, which bear only a single real egg in the anterior part of the gonad, to such possessing an ovary behind which lies a small testicular part. In any case, however, only a part of the reproductive organ is functional and the rest, presenting the character of the other sex, is a functionless rudiment. We could regard this case as bisexuality with accessory hermaphroditism of both sexes. It is a pity that the example scarcely lends itself to experiment.

It is quite likely that interesting discoveries may be expected in connection with investigations on fishes. Some notes by Grassi[3] on the development of the reproductive organs in the eel suggests that possibly conditions occur here similar to those in the Amphibia. A note by Julian Huxley[4] on the sex ratios of *Girardinus* may also be interpreted in this way.

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[1] Harms, W., "Verwandlung des Bidderschen Organs in ein Ovarium beim Männchen von *Bufo vulgaris* Laur." Zool. Anz., 55, 1921.—Harms, W., "Untersuchungen Über das Biddersche Organ bei männlichen und weiblichen Kröten." Ztschr. Anat. Entwicklung., 62, 1921.

[2] Schreiner, K. E., "Über das Generationsorgan von *Myxine glutinosa* L." Biol. Centrbl., 24, 1904.

[3] Grassi, B., "Nuove ricerche su la storia naturale dell' *Anguilla*." R. Com. talassograf. Ital. Mem., 47, 1919.

[4] Huxley, J. S., "Note on an Alternating Preponderance of Males and Females in Fish and its Possible Significance." Journ. of Genetics, 10, 1920.

2. Accidental Hermaphroditism

Giard has used the term accidental hermaphroditism for an abnormality occasionally met with where sperm tissue is found within an ovary or eggs within a testis. The latter condition occurs amongst the most different groups of the animal kingdom.[1] It is particularly common amongst Crustacea (see Fig. 88), but the Amphibia and Mammalia also present cases. Local sperm formation in an otherwise normal star fish ovary is illustrated in Fig. 89. Corresponding cases are known in fishes and in *Apus*. One has found eggs even in the testis of the hermaphrodite Ascidian *Fragarium*. It is clear that this kind of thing would be of the greatest physiological importance if one could take it in hand experimentally. That in principle any primordial germ cell can develop into either a spermatozoon or an egg has been demonstrated by the intersexuality investigations. But it was always the physiological condition of the

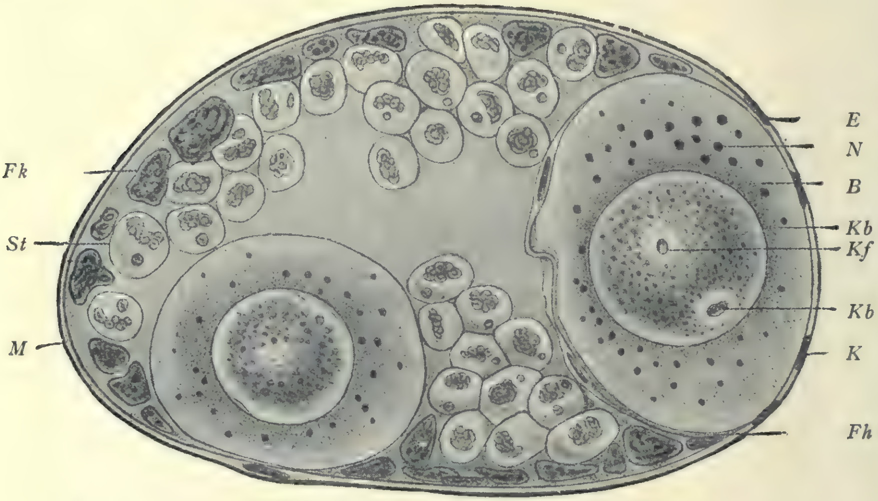

FIG. 88.—Acinus of testis with eggs from a ♂ specimen of *Potamobius astacus*.

B, egg plasm; E, egg; Fh, follicular membrane; Fk, follicle nuclei; Kb, germinal vesicle; Kf, nucleolus; M, membrane of testis acinus; K, nucleus of the same; N, yolk St. Spermatogonia.

After La Valette-St. George.

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[1] Krohn, E., "Die Zeugungsorgane von *Phalangium*, Arch. Naturgesch.," 1865.—Harms, l.c.—Agar, "The Spermatogenesis of *Lepidosiren*." Qu. J. Micr. Sc., 57, 1911.—Buchner, P., "Über hermaphrodite Seesterne." Zool. Anz., 37, 1911.—Redikorzew, W., "Die Zwitter-drüsenbildung einer zusammengesetzten Ascidie." Zool. Anz., 25, 1902.—Cuénot, S., "Notes sur les Echinodermes, III." *Ibid.*, 21, 1898.

whole organism which decided the direction the development should take.

Here, however, in spite of the sexual normality of the individuals, the elements of the other sex are developed in one or a few localized spots. Clearly this is a problem that should lead us another step further in the analysis of the physiology of sex.

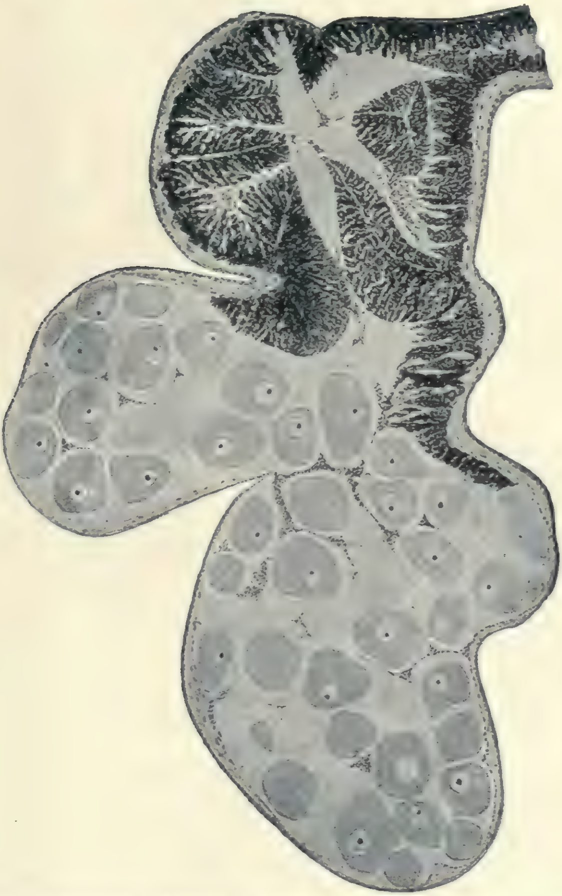
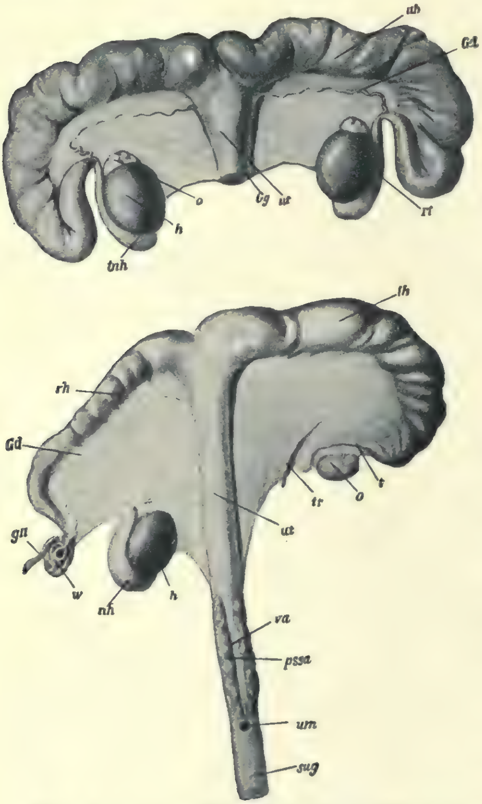


Fig. 89.—Section through the ovary of a star fish with testis tissue. After Buchner.

In connection with the observations on parasitic castration it has already been shown how the action of the sex differentiating hormones must be regarded. It appeared most probable that the action of the hormones was related to the general metabolism, and that the specific metabolic condition called forth was itself the ultimate and direct cause of the morphological differentiation towards one sex or the other. If such be the case, it indicates that in the examples now under discussion a chemical situation can arise at local places independent of the hormones dominating the general physiological state of the body, and this local state of affairs is of the same nature as that called forth by the contrary hormones. An experimental control of this phenomenon would explain this, perhaps the last, problem of sex differentiation. It is, however, still beyond our reach. Naturally one would have first to make certain that it was not a phenomenon belonging to our group accessory hermaphroditism.

3. Teratological Hermaphroditism

It is possible that this section will later be shown to be logically untenable. Essentially it comprises cases for which no biological explanation can be given, and which therefore must be regarded as abnormalities until we know something of their cause. Some day perhaps they may attain to such an importance as the case of the freemartin. The examples to be placed in this category are the hermaphrodites occurring occasionally as monstrosities in the most diverse animal groups, and especially in birds and mammals. Sex glands are present which usually have ovarial and testicular regions side by side and more or less distinctly marked off from each other. The other genitalia present all sorts of combinations of the two sexes. Very frequently the two sides of the body in these cases are somewhat asymmetrical, and



Figs. 90 and 91.—Semi-diagrammatic illustration of the internal genitalia of pig hermaphrodites.

Gd, vas deferens; gh, gubernaculum Hunteri; h, testis; nh, epididymis; o, ovary; pssa, pseudo-seminal vesicle; rt, right oviduct; sug, sinus urogenitalis; t, oviduct; tr, lig. rotundum; uh, horn of uterus; um, opening of urethra; ut, uterus; va, vagina; w, knot about vas deferens.

After Pick.

since in at least one of these examples (an hermaphrodite pheasant described by Bond (l.c.)) the secondary sexual characters of the right and left halves of the body were different, it is possible that some form of gynandromorphism is present—that is, a genetic mosaic.

The general nature of these hermaphrodites is illustrated in Figs. 90 and 91 (after Pick) representing pig hermaphrodites. (For comparison see the diagram of the mammalian urino-genital apparatus, Fig. 110.)

In Fig. 90 there is present, in addition to the vagina and uterus, a testis, epididymis and vas deferens, and to each testis a hood-shaped ovary is appended. Fig. 91 represents a similar condition but the asymmetry is greater. On the right side a testis is present, on the left an hermaphrodite gland with the appearance of an ovary.

In regard to Steinach's investigations reference should be made to the section on hermaphroditism in man (pp. 248).[1]

B. Functional Hermaphroditism or Monœcism

As was pointed out in the introduction to this section, real hermaphroditism or monœcism is an experimentally almost unknown field in the animal kingdom. A definite classification of the facts is scarcely possible therefore, and the following attempt to clear matters a little, must be regarded as merely of a preliminary nature. When we glance over the very varied and biologically remarkable facts of monœcism three different groups seem to be present. In the first an individual belongs permanently to only one sex genetically. The monœcious condition is expressed either in the fact that a real female, in spite of its female organization, produces spermatozoa temporarily (gynomonœcious condition) or the converse (andromonœcious condition) is the case. We could speak of this, therefore, as unisexual monœcism. In the second group the individuals are first male then female; genetically these are probably males (consecutive monœcism). In the third group the individuals possess permanently the two kinds of sex organs side by side—that is, are spacially monœcious. Naturally this does not exclude the possibility that one kind of germ cell ripens earlier than the other. Perhaps this group is only a special variety of the foregoing one. Anyway, as pointed out above, all this is only a preliminary effort at classification.

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[1] Bond, C. T., "On a Case of Unilateral Development," etc. Journ. Genetics, 3, 1914.—Pick, L., "Über den wahren Hermaphroditismus des Menschen." Arch. Mikr. Anat., 84, 1914. (An extensive list of literature is given.)

1. Unisexual Monœcism

The most frequent form of unisexual monœcism appears to be gynomonœcism. The Nematode *Angiostomum nigrovenosum* may be taken as a type of this group. It is known that in this worm a free living generation, in which the sexes are separate, alternates with a parasitic hermaphrodite form in the lung of the frog. Now since the anatomical structure of the two sexes in the Nematoda is typically different, whilst at the same time there is a remarkable uniformity in the group, it is easy to determine that the hermaphrodite animals are anatomically females. But they produce eggs and spermatozoa alternately in their ovarial tubes—in other words they possess an hermaphrodite gland (Fig. 92).

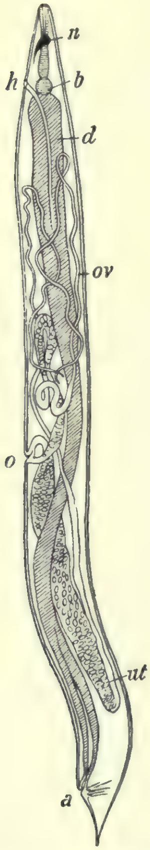

Fig. 92.—*Angiostomum nigrovenosum* from the lung of the frog.

a, anus; b, pharynx; d, alimentary canal; h, excretory pore; n, nerve ring; o, reproductive aperture; ov, ovary; ut, uterus. From Goette.

This case has been investigated cytologically by Schleip and Boveri[1] with the following results (see diagram, Fig. 93): "The females of the bisexual generation possess (at least in the germ cell lineage) cells with twelve chromosomes and they produce eggs with six chromosomes. The males have only eleven chromosomes and produce spermatozoa of two kinds, that is some with six and some with five chromosomes, both of which are transferred at fertilization to the receptaculum of the female. In spite of this, only the spermatozoa with six chromosomes can fertilize the eggs, a fact which is placed beyond doubt when we find that the cells of the succeeding generation always possess twelve chromosomes. This generation, the parasitic and hermaphrodite generation from the frog's lung, consists of individuals all of which must be regarded (from the anatomical structure of the body) as females. Such an assumption is in agreement with the fact that they possess the same chromosome number as the females of the bisexual generation. These individuals produce, however, both eggs and spermatozoa and several lots of these alternate, the cells of the synapsis zone developing partly as oocytes and partly remaining rather small and giving rise to spermatozoa. In the maturation of the oocytes no special peculiarities are to be noted, and all the mature eggs possess the reduced number of chromosomes, namely, six. In the spermatocytes, however, one chromosome differentiates first and then a second. These are the two accessory chromosomes which appertain to the female sex. They remain unpaired, whilst the other ten chromosomes differentiate from the resting stage as five double chromosomes. The first maturation division is the reduction division for these, the second one the equational division. And thus in each spermatid there comes to be five ordinary chromosomes. The accessory chromosomes remaining unpaired are first split longitudinally and then at the second division one goes to each spermatid. But only in one spermatid does it unite with the five autosomes, in the other it remains in proximity to the equatorial plane, and when the sperm separates from its residual body the chromosome remains in the latter. Presumably the accessory chromosome which is thrown out is the one which is the most abnormal in condition—thus the one which becomes compact in the spermatocyte. We see then that in these hermaphrodites also two kinds of spermatozoa are developed, some with five and others with six chromosomes, and they are produced in equal numbers. Thus it is easy to understand that the male of the bisexual generation contains eleven chromosomes and the female twelve chromosomes" (Schleip).

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[1] Schleip, W., "Das Verhalten des Chromatins bei *Angiostomum* (*Rhabdonema*) *nigrovenosum*." Arch. Zellf., 7, 1911.

These facts are really sufficient to introduce us to the principal features of gynomonœcious hermaphroditism and an understanding of the same. The parasitic hermaphrodites are here genetically females, as the anatomy and chromosome conditions clearly indicate. The mechanism which determines that these alone shall arise from the fertilized eggs is the one so well known in other cases (Aphids)—the restriction of the capacity of fertilization to only one kind of spermatozoa. These parasitic females possess the ability to produce both eggs and spermatozoa from their primordial germ cells. In other words, a condition which we found present as an abnormality in the case treated under the head of accidental hermaphroditism occurs here as the normal and permanent state. The explanation might quite well be the same—that it is determined by particularly localized chemical conditions. Although we cannot define these conditions as yet, the case belongs to the problems which we have previously discussed in connection with parasitic castration. It is a very striking fact, too, that in the male germ cells of the parasitic worm a chromosome is destroyed resulting in the possibility of digametism again. It is perhaps less striking if we assume that the protoplasm of the sperm cells (a product of the supposed specific chemical conditions) has also specific peculiarities, and we recollect that Boveri[1] has shown that the chromatin diminution in *Ascaris* is determined by the protoplasmic constitution.

The other cases which belong to this group of phenomena agree essentially, so far as details are known, with the interpretation suggested here. They include in the first place the free living Nematodes which are known to be protandric hermaphrodites.[2] These are without doubt females whose reproductive organs have for a time the faculty of producing spermatozoa. Maupas clearly established the fact that this feature is limited to a small number of cells which are soon exhausted. As far as the details are concerned we are introduced to very interesting conditions here, and in regard to which further experimental material is much to be desired. For example, in addition to these gynomonœcious forms, some males occur simultaneously, although only rarely (a fact which supports our idea that the gynomonœcious forms are genetically females). The percentage of these males varies according to the species. Generally they have lost the instinct of fertilization. If, however, they do attain to this, it may or may not have an effect on the number of males in the offspring.

Investigations made by Krüger on a form of this kind (see later) make it very probable that these last conditions are related to the chromosome mechanism and correspond to expectations. The protandric condition is thereby naturally not affected. So far as our knowledge permits of a certain conclusion, the hermaphrodite molluscs also belong to this group, although at first sight this does not seem very probable. A decision on an experimental as well as on a cytological basis has of course not yet been made. There are some discoveries of Demoll[1] for Helix, as well as those of Zarnik[2] for Pteropoda, which have been taken by the authors as indicating that the male germ cells are of two kinds but that only one sort fertilizes the eggs. The hermaphrodites would thus be genetically females. We must abstain, however, from giving the details, since they do not seem quite in harmony with each other. At the same time it is noteworthy that, from the point of view of comparative morphology, one has arrived at the conclusion that these hermaphrodites are gynomonœcious, and Pelseneer has adopted this point of view[3] and endeavoured to establish it. The difficulty is not so great in species where differentiated gonoducts and copulatory apparatus are absent.

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[1] Boveri, Th., "Die Potenzen der Ascarisblastomeren bei veränderter Furchung." Festschr. f. R. Hertwig, 3 B., 1910.

[2] Maupas, E., "Modes et formes de reproduction des Nematodes." Arch. Zool. Exp. III., S. 8, 1900.

So the fact that there are oysters and Pectens which are protandric hermaphrodites whilst others have the sexes separate seems highly significant if we put it together with the conditions found in free living nematodes, conditions which lead us to the assumption that the hermaphrodites are females.

The difficulties arise in regard to the facts that in the hermaphrodite Gastropoda both kinds of secondary sex characters are present, although Pelseneer points out in this connection that in the Pulmonata the male gonoducts are only secondarily added to the female and that the absence of the male parts is a frequent abnormality, whilst the converse never occurs. Still, as we stated above, a conclusion firmly established on experiment is lacking. Furthermore it is not possible to deduce any certain conception from the available biological data. Very many pulmonates are protandric, in others the two kinds of germ cells are brought to maturity during the whole life of the animal (*Helix arbustorum* according to Buresch), whilst Babor[1] finds that in *Limax maximus* the individuals are first female, then hermaphrodite, then male, then again hermaphrodite, and finally once more female.

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[1] Demoll, R., "Die Spermatogenese von *Helix pomatia* L." Zool. Jahrb. Suppl., 15, 1912.

[2] Zarnik, B., "Über den Chromosomencyklus bei Pteropoden." Verh. deutsch. Zool. Ges., 1911.

[3] Pelseneer, P., "Hermaphroditism in Mollusca." Quart. Jour. Micr. Sc., 37, 1894-95.

The physiological interest in this case is naturally focussed on the production of two kinds of germ cells in an hermaphrodite gland, as is the case in the majority of these molluscs (it may even be within the same acinus, as for example in the Valvata, *Ostrea*, Pulmonates, and Neomeniidæ). The maturation of these different germ cells usually does not take place simultaneously; generally there is protandry, in the case of *Limax*, however, proterogyny. In regard to the conditions underlying the differentiation of both sorts of germ cells we know at least a very little. Both Ancel and Buresch[2] have shown that the same primordial germ cells may become eggs or spermatozoa according as they enter into relations with so-called nurse cells or not. What this means physiologically we do not know. An indication is given perhaps by the following. We were able to show[3] that the differentiation of a sperm cell into a spermatozoon was to a certain extent controlled by osmotic conditions whose regulation was a function of the follicle cells—and these are probably related physiologically to the nurse cells of the eggs.

All this leaves us, however, in the dark regarding the physiological basis of gynomonœcism. What is it that distinguishes such females from normal females? The conception of special quantitative conditions or reaction conditions of the sex enzymes does not suffice as an explanation. The special physiological condition, with its localized mosaic-like or temporal variations, must rest somehow on a peculiarity of genetic constitution which up to date is both mechanically and physiologically unknown. Nor is it explained by the phrase—Factor for Monœcism.

Andromonœcism appears to be much more rare than gynomonœcism; it was claimed to be the state in *Bradynema rigidum* amongst the Nematoda, but recent unpublished investigations by Wülker prove that this is not the case. Thus far no exactly analysed case is known.

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[1] Babor, J., "Ein. Beitrag zur Geschlechtsmetamorphose." Verhdlg. Zool. Bot. Ges. Wien, 1898.

[2] Ancel, P., "Histogénèse et structure de la glande hermaphrodite *d'Helix pomatia*." Arch. Biol., 19, 1903.—Buresch, J., "Untersuchungen über die Zwitterdrüse der Pulmonaten." Arch. Zellf., 7, 1912.

[3] Goldschmidt, R., "Untersuchungen über spermatogenese in vitro." Arch. Zellf., 14, 1917.

2. Consecutive Monœcism

The most important examples of this group are to be found amongst the Isopod Crustacea in the feebly parasitic group of the Cymothoidæ and the parasitic Epicaridea.[1] The main feature is that every individual as a free living larva is a male and copulates with the parasitic female. Then it attaches itself and becomes transformed into a female. *Danalia*, one of the Liriopsidæ, which is parasitic on another parasitic Crustacean (a Rhizocephalan), will serve as an example. Out of the eggs of these parasites free swimming larvæ develop termed Cryptoniscus larvæ, and these are the functional males. They seek a grown-up female and fertilize it, after which they become fixed themselves. The morphological transformations which they now undergo consist of an entire alteration in form and the assumption of the female organization. All the male parts are completely destroyed by phagocytes (the reader is reminded here of our remarks on phagocytism and chemistry on an earlier page) and then the female organs develop. The male larva had, as a matter of fact, also a fundament (*anlage*) of the ovary at the anterior end of its reproductive organs (Fig. 94). The conditions in the other parasitic Isopods with consecutive monœcism are essentially the same in principle.

Geoffrey Smith in particular has maintained that all these hermaphrodites are genetically males. He arrived at this conclusion after comparisons with the phenomena (already described in this work) which occur elsewhere in the group Crustacea, namely, the transformation of the parasitically castrated *Inachus* males, and the presence of portions of ovarial tissue in the testis in some species (*Orchestia*, *Gebia*); and in connection with his general views on sex determination by special metabolic conditions. To substantiate this view he brought forward certain facts which have not been discussed so far, but which are very interesting.[1] In certain species of crabs one finds three kinds of males during the breeding season (Fig. 95). There are small males with swollen chelæ, average-sized individuals with compressed chelæ, and large specimens with very much swollen chelæ. The first and last of these are sexually completely normal, but the other type with a rather female type of chela contains shrunken testes with few spermatozoa. Geoffrey Smith compares this condition with the sexual dimorphism of certain Lamellicorn beetles, in which small males with feebly developed secondary sex characters occur together with the

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[1] Mayer, P., "Carcinologische Mitteilungen," 6. Mittl. Zool. St. Neapel, 1, 1879.—Caullery, M., "Recherches sur les Liriopsidæ," etc. *Ibid.*, 18, 1908.—Bonnier, J., "Contribution à l'étude des Epicarides." Trav. Wimereux, 8, 1900.—Smith, G., "Rhizocephala." Naples Monogr., 29, 1906.

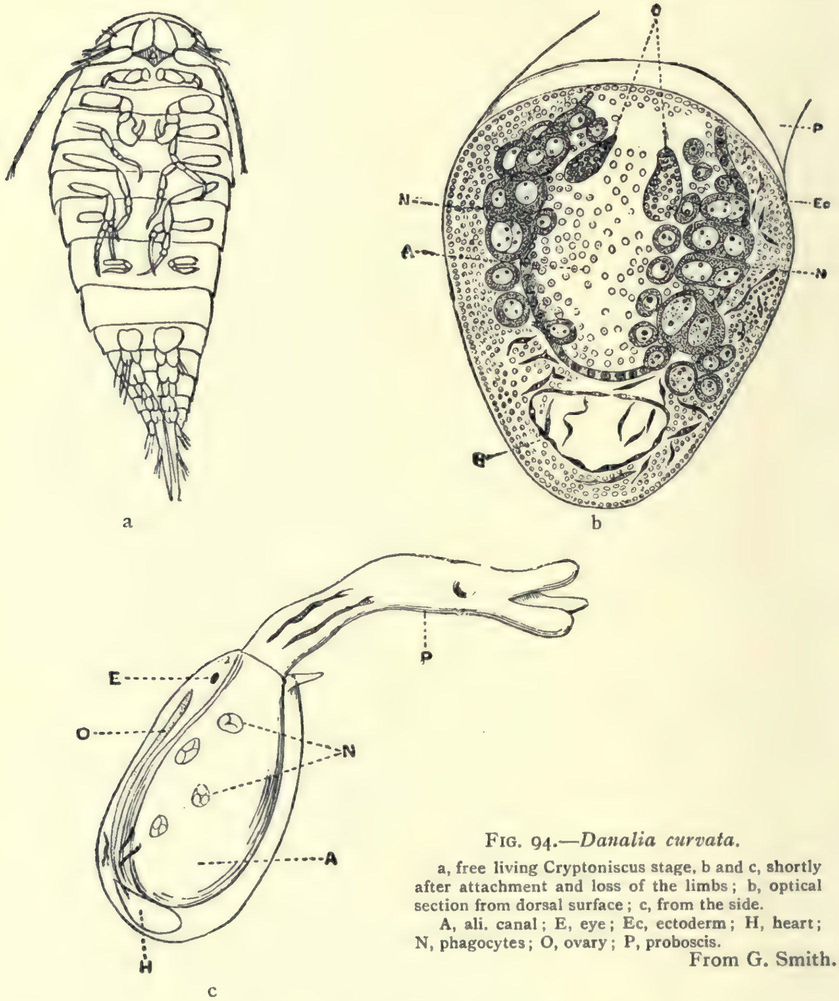

FIG. 94.—*Danalia curvata.*

a, free living Cryptoniscus stage, b and c, shortly after attachment and loss of the limbs; b, optical section from dorsal surface; c, from the side.

A, ali. canal; E, eye; Ec, ectoderm; H, heart; N, phagocytes; O, ovary; P, proboscis.

From G. Smith.

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[1] Smith, G., "High and Low Dimorphism." Mittl. Zool. St. Neapel, 17, 1905.

normal large individuals. The middle-sized crabs are regarded as animals in a condition of rapid growth accompanied by a repression of sexual maturity. Smith concludes that the male Crustacea have the faculty of passing into a kind of hermaphrodite condition when the metabolic activity increases at the expense of the sexual activity. This change is supposed to take place in the case of the Isopods mentioned above through a transition to parasitic habits.

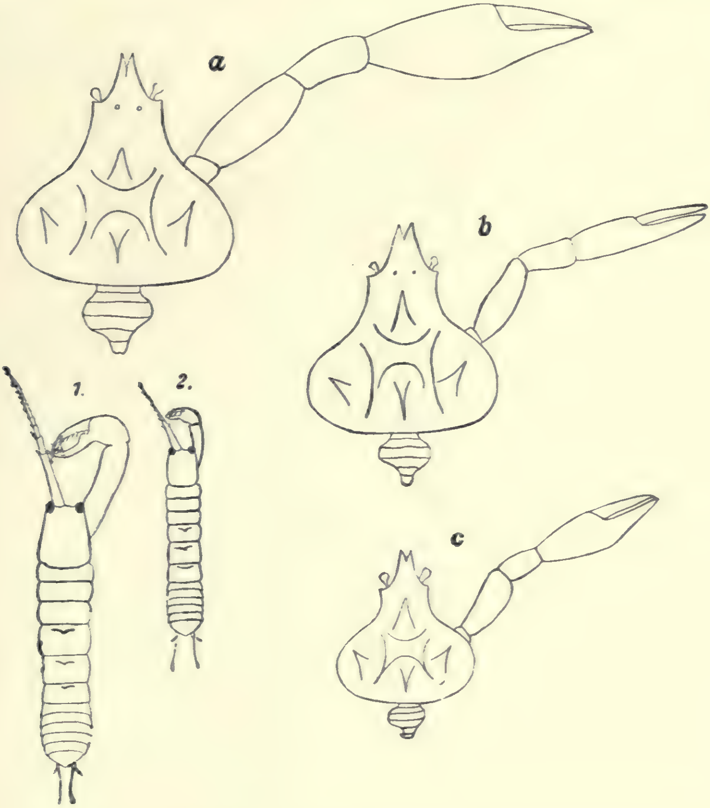

FIG. 95.—1, 2, two male forms (" high " and " low ") of *Leptochelia dubia*. a, b, and c, the three male types of *Inachus thoracicus* (high, middle, and low). After G. Smith.

In regard to these Crustacea we have up to date no investigation which would enable us to take up a definite point of view.

On the other hand, we may perhaps obtain a better idea of the conditions if we look into the interesting biology of certain Prosobranch Molluscs which have been studied biologically and experimentally by Conklin, Orton, and Gould.[1] In the family Calyptræidæ species of the genus *Crepidula* are met with which are almost or completely sedentary, fixing themselves during their life on oyster shells or on the Gastropod shells inhabited by hermit crabs. These forms appear without exception to present the condition termed protandric hermaphroditism. Every individual is first a male both functionally and structurally, then the male organs suffer a retrogression whilst the female organs develop so that a kind of hermaphrodite condition arises. Eventually a purely female stage is reached.

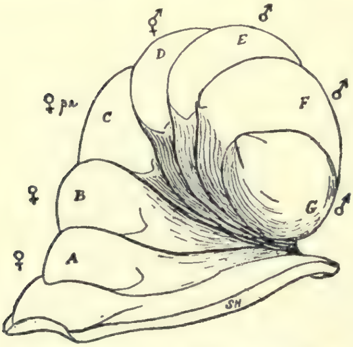

FIG. 96.—Chain of *Crepidula fornicata* growing attached to a shell SH. From A-G the individuals range from females through hermaphrodites to males. After Orton.

The sequence is particularly clear in those species which form chains—a new coming larva attaching itself to an already fixed animal, and so on. In these chains the oldest and largest animals are females, the middle members of the series are hermaphrodites in different stages, and the youngest and smallest individuals are males (Fig. 96).

In one of these species, *Crepidula plana*, Gould discovered very remarkable conditions. Young animals which were found fixed on recent cells were generally neutral. Now if these were kept by themselves (and the same thing applies to the males) they soon developed into females. If, however, these young neutrals were brought into the proximity of older animals (it matters not whether they be males or females) they passed at once into the male phase. All the experiments showed that the presence of the larger and older animals was necessary to bring about the development of the male condition. Larvæ which develop without the presence of the larger individuals probably never run through a male phase at all, but it can be induced at any time during a rather long period of development if large animals are added. And after the male phase is over, when the animal is passing through the intermediate phase towards the completely female period, the male condition can to a certain degree be repeated if the stimulus (the presence of large neighbours) is repeated. The experiment, however, does not succeed after the female phase has been really entered.

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[1] Conklin, E. G., "Environmental and Sexual Dimorphism in *Crepidula*." Proc. Ac. Nat. Sc., Philadelphia, 1898.—Orton, J. H., "On the Occurrence of Protandric Hermaphroditism in the Mollusc *Crepidula fornicata*." Proc. R. Soc., London, 81B, 1909.—Gould, H. N., "Studies on Sex in the Hermaphrodite Mollusk *Crepidula plana*." I. Journ. Exp. Zool., 23, 1917. II. *Ibid.*

During the male phase the growth of the body is retarded; it is, however, very rapid in neutrals and likewise in animals which have passed the male phase. No discoveries have, however, been made which explain the kind of stimulus exerted by the large animals.

When these interesting discoveries are considered and an effort is made to seek an interpretation, it strikes one that the different velocity of growth of the neutral and female phases compared with that of the male phase is a point of some importance. We have again to deal with the important factor, the velocity of differentiation whose significance has been made evident in our discussion of intersexuality. And here we see in what lies the mysterious influence of the large animals—they slow down the differentiation. What causes this is unknown, Gould could obtain no positive results, but the fact is of great significance, for it allows us to establish a connection with the phenomena of intersexuality. The situation is then as follows: (1) In the other species of *Crepidula* we find that, just as in the Crustacea mentioned above, every individual develops first as a male. (2) In both cases these males are free swimming or mobile, whilst the later female phase is sedentary, parasitic or commensal. (3) In *C. plana* the male phase only occurs when the development is retarded through the presence of larger animals.

The same genetic conditions must therefore exist in all the cases, and the special peculiarity of *C. plana* lies only in the fact that the physiological conditions determining the female phase, which are called forth by parasitism or commensalism, are reached with great speed provided that the retarding influence of larger neighbours is lacking. Recall for a moment the explanation of the normal and intersexual males of *Lymantria*. In this case normal males developed when the more slowly running production of female hormones (compared with the hormones of male differentiation) reached a working quantity only after the conclusion of development. If the point where an efficient quantity of female hormones was available occurred *within* the period of development, an intersex was the result. Suppose now that such a male butterfly was able to take up a parasitic life and to continue to grow—it would undergo a transformation into a female.

We suggest, therefore, that these consecutive hermaphrodites are genetically males whose existence is as it were extended beyond their normal life's duration as an effect of parasitism or commensalism, so that they actually live to see their female phase. Any insect would respond in a similar manner if it was in the same physiological position, and so also would the Amphibia; and the birds and the mammals too if the internal secretion of the gonads did not continually repress the opposite sexual phase. Thus we could express the conditions of consecutive hermaphroditism with the curve (Fig. 97) now so familiar to us. It is adapted to all the cases named. For *Crepidula plana* there is the additional fact that the velocity of differentiation from the beginning is so great that the male phase only attains to clear development when this speed is retarded through the unknown influence of the presence of larger animals. This is the manner in which we understand, at least in principle, the important conditions of this group of facts.

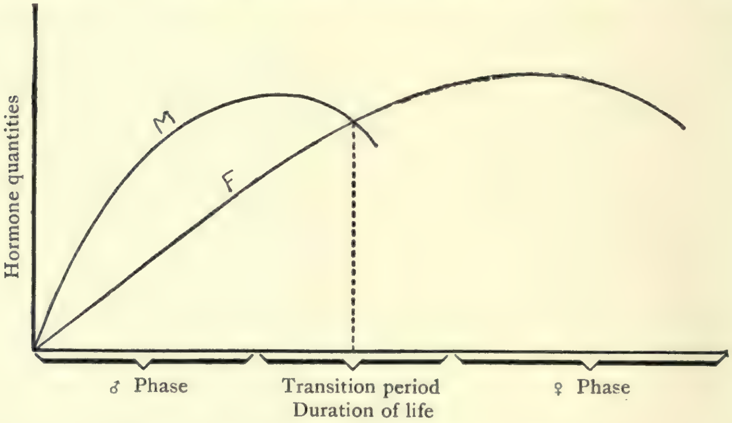

FIG. 97.—Graph of the sexual cycle of *Crepidula*.

It is not improbable that the peculiar hermaphroditism of *Asterina gibbosa* discovered by Cuénot[1] belongs also to this group. It is a type of hermaphroditism which comes out differently in different geographical situations. At Roscoff every individual is first male and then a female for the rest of its life.

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[1] Cuénot, L., "Notes sur les Echinodermes, III." Zool. Anz., 21, 1898.

At Banyuls the state of affairs is similar, but the two periods overlap to a greater extent. At Naples the different types occur irregularly. An experimental analysis of this case would be very interesting.

We have thus put forward the view, as did Geoffrey Smith, that the consecutive hermaphrodites are genetically males. It must, however, be emphasized that it is possible to look at them in another way. The proof that they are genetically males can only be considered as demonstrated when it is shown that two sorts of eggs or two sorts of sperms are produced of which one kind only functions. The term "genetic male" has no meaning if genetic females are not also conceivable. But it is also possible that these hermaphrodites are genetically neither females nor males—that is to say that all the gametes are capable of function and equivalent, and every fertilization results therefore in the same combination so far as the quantitative condition of the sex enzymes is concerned. We should then have to deal with a third sex.

3. Spacial Monœcism

Spacial monœcism is the state of hermaphroditism in the narrowest sense, the presence of both kinds of sex organs with the totality of their accessory organs side by side in the same individual. So far there is no weighty reason for regarding these hermaphrodites as modifications of one sex, they are much more like mosaic formations of both sexes. Thus we shall not be surprised to find in such forms—certain Oligochetes, Turbellaria, Trematoda, and Cestoda—no cytological specialities, for these are bound up with the mechanism of the differentiation of two sexes. Upon what genetic or physiological basis this monœcious condition rests we do not know, since experimental evidence is up to the present lacking, and it is not altogether without danger to draw conclusions regarding the animal kingdom from the conditions found in monœcious plants, as Correns[1] in particular has pointed out.

If, however, there is anything in the animal kingdom which *does* resemble the monœcism of the plants, it is in the group we are discussing here. And the following facts also support this. In several groups of monœcious animals one meets with the remarkable phenomenon of complementary males which are more or less regularly found side by side with the hermaphrodites which are practising cross fertilization. The classic examples are the Cirripedia. In the case of *Scalpellum vulgare*, for example, one always finds a number of tiny males (which

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[1] Correns, C., "Über den Unterschied von tierischem und pflanzlichem Zwittertum." Biol. Centralbl., 36, 1916.

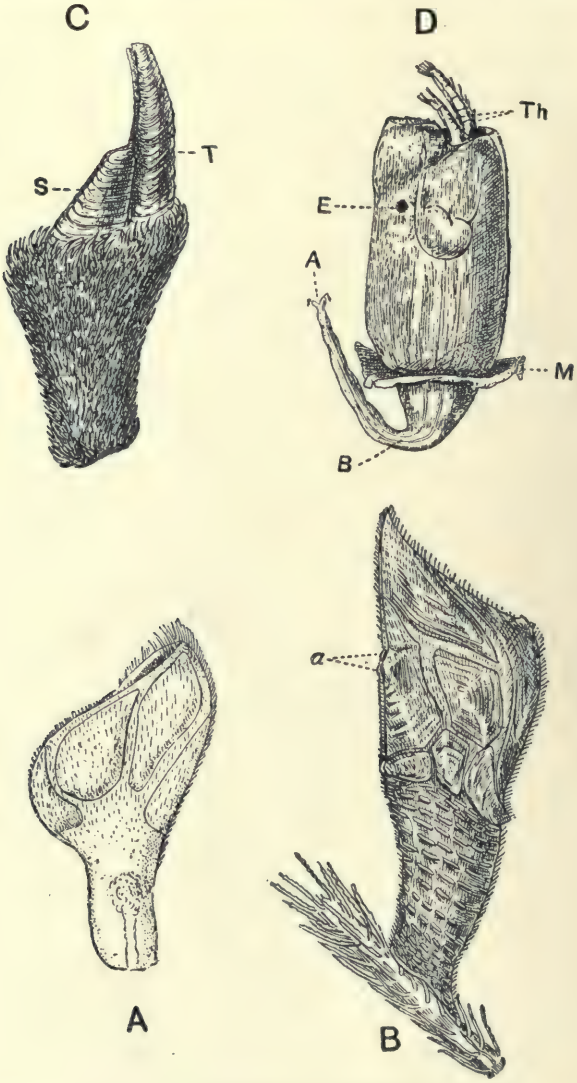

FIG. 98.—Cirripedia—sexual individuals.

A, complementary males of *Scalpellum peronii*; B, hermaphrodite individual of *S. vulgare*, a, attached complementary males; C, ♀ of *Ibla cumingii*, S, Scutum, T, Tergum.

D, dwarf male of the above; A, antennæ; B, projects into the ♀ to which the piece of skin M belongs; E, eye; Th, thoracic appendages.

After G. Smith.

Darwin[1] termed complementary males) in the mantle cavity of the hermaphrodites. These are small rudimentary Scalpellums whose anatomy consists of little else but reproductive organs (Fig. 98). Now it is worthy of note that there are several related species—of *Scalpellum* as well as of the related genus *Ibla*—where the sexes are separate and consist of females and dwarf males like the complementary males. The significance of these facts is made a little more clear perhaps by conditions found in other hermaphrodite groups. Thus in *Myzostoma* one always finds a larger and a smaller animal together, the latter being a complementary male. Now Wheeler showed[2] that every individual developed the male organs first, before it

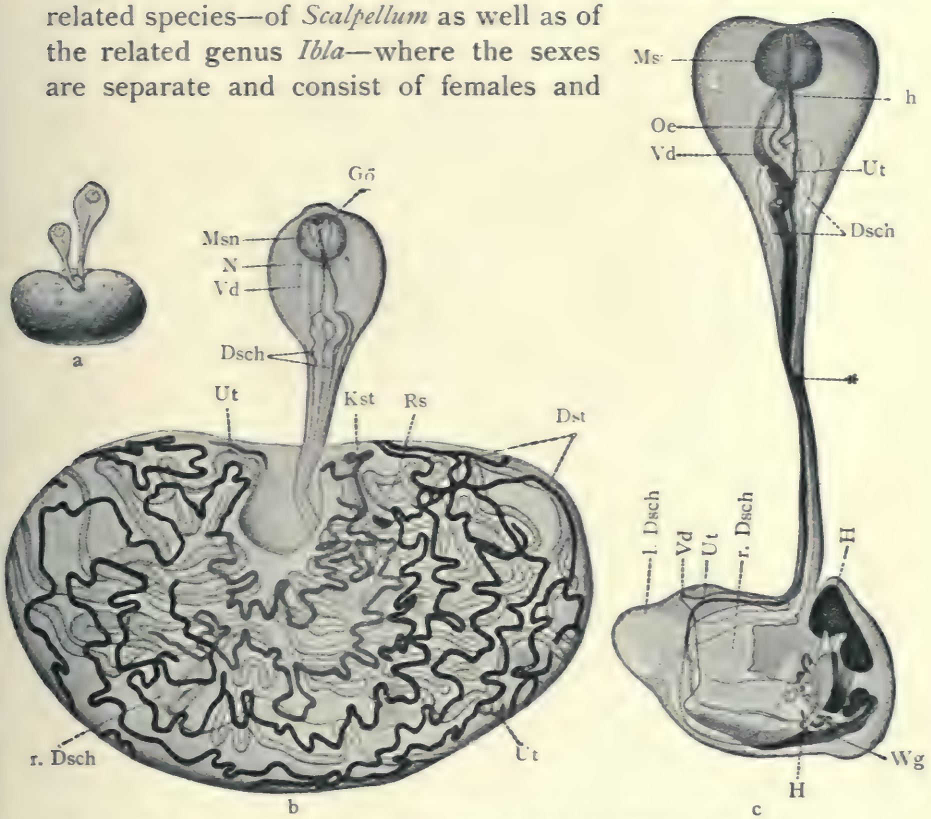

FIG. 99.—*Wedlia bipartita*; a, ♀ with attached ♂ ♂; b, ♀ more highly magnified; c, ♂ ditto.

Dsch, ali. canal branch (l and r = left and right); Dst, vittelarium; Gö, genital aperture; H, testis; Kst, ovary; Msn, oral sucker; N, central nervous system; Oe, œsophagus; Ph, pharynx; Rs, recept. seminis; Ut, uterus; Vd, vas deferens; Wg, rudimentary female genital complex.

After Odhner from Goldschmidt.

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[1] Gruvel, "Monographie des Cirrhipèdes." Paris, 1905.

[2] Wheeler, E. M., "The Sexual Phases of *Myzostoma*." Mitt. Zool. St. Naples, 12, 1897.

appeared as a real hermaphrodite, and that consequently the complementary males must be regarded as nothing else but hermaphrodites which have remained at an earlier developmental stage. This is shown more beautifully still in the Trematode group of the Didymozoa, where hermaphrodite animals have become males or females through the rudimentation of one set of organs (Fig. 99). These animals even present sexual dimorphism ; the dwarf males are attached to the females.[1]

Two hermaphrodites can thus appear secondarily as male and female individuals through repression of the organs of the opposite sex. A time factor is also concerned here, for the male organs are normally ready first and the female organs still function when the former are exhausted. This point will be of importance in future experimental investigation. In any case it makes it probable that the complementary males are hermaphrodites, and that in representatives of this group where the sexes are separate the dwarf males are also to be regarded in this light, whilst the females correspond to old hermaphrodites. And for the males at least it is possible to bring forward the fact that the complementary males of *Scalpellum peronii* produce egg cells in the testis. Finally, it may be noticed that Geoffrey Smith upheld the view that these Cirripedes also were really males and thus andromonœcious. The accuracy of this view can neither be disputed nor supported at the present moment. It is not impossible that these monœcious cases have the same genetic basis as those of the former group, with the single difference that the appearance and functioning of the organs of one sex do not disturb the action of those of the other sex.

SUMMARY

It appears desirable, in concluding this section, to bring together again the very different sets of conditions which have been and are described under the title of hermaphroditism. The common resemblance in the various cases is that both kinds of sex cells are produced in the same individual, but genetically and physiologically there are groups which are quite different. The group of hermaphrodites will probably almost disappear from animal biology when the phenomena involved in the individual cases coming under this head at present are completely explained.

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[1] Odhner, Th., "Zur Anatomie der Didymozoen." Zool. Stud. til. Prof. Tulberg. Upsala, 1907.

1. *Intersexuality.*—An intersex is an animal which is genetically a male or a female and which, through physiological or genetic causes, has changed its sex at a particular moment in its development. Certain stages, therefore, in an intersexual may fall under the term hermaphroditism.

2. *Gynandromorphism.*—A gynandromorph is a mosaic formation in regard to sexual differentiation, determined by abnormal cytological conditions, which transmit to many groups of cells the chromosome combination of the one sex and to others that of the opposite sex. If the sex organs themselves are developed from (one might say covered by) two such cell groups, an hermaphrodite condition is the result.

3. *Accessory Hermaphroditism.* — In addition to the testis a rudimentary ovary is developed, which, however, is sexually functionless. The conditions are physiologically very close to certain types of intersexuality.

4. *Accidental Hermaphroditism.*—Egg cells occur sporadically in the testis and spermatic tissue in the ovary. The cause is unknown, special local abnormal chemical conditions are possible.

5. *Teratological Hermaphroditism.*—Hermaphrodite individuals occurring as abnormalities in a bisexual species. If the cause of their origin were known, they would probably have to be arranged in one of the other groups (probably under the head of gynandromorphism).

6. *Unisexual Monœcism.*—A female (or male) animal develops at certain times spermatozoa in the ovary (or eggs in the testis), the result of which is that the other sex becomes superfluous and more or less disappears. Special biological conditions go hand in hand with the phenomena. (Certain Nematoda and probably also the hermaphrodite molluscs belong to this group.)

7. *Consecutive Monœcism.*—Every individual is first male then female. Genetically the organisms are males or neutrals. The phenomenon is combined with special biological conditions (parasitism, sedentary mode of life) and is physiologically closely related to intersexuality.

8. *Spacial Monœcism.*—The real, functional hermaphroditism (of certain Oligochæts, Cestoda, Trematoda, etc.) whose genetic basis is still unknown. The future may see it classed under the groups 6 or 7.

CHAPTER VI

PARTHENOGENESIS AND SEX

THE relations between parthenogenesis and sex form one of the most familiar phenomena of sexuality, and one which in many animal groups is perhaps the most striking and most discussed part of their biology.

Any solution of the sex problem must therefore provide a sufficient explanation of these conditions; in fact these phenomena should to some extent be used as a test. As a matter of fact the phenomena fit in completely with the knowledge already gained, as will appear in the following subsections.

A. PARTHENOGENESIS AND THE MECHANISM OF SEX DISTRIBUTION

We know that the normal mechanism for sex distribution is the chromosome mechanism which controls or regulates the quantitative relations of the sex enzymes. If, then, a special distribution of the sexes is found in conjunction with parthenogenesis, it would be explained if a corresponding chromosome mechanism could be demonstrated. Let us commence with the basis of our earlier discussions regarding this mechanism and its significance. Two types had to be distinguished—the one with female and the other with male heterozygotism. In the first type the formula adopted was (F)Mm = ♀, (F)MM = ♂, meaning that in terms of the sex chromosomes the presence of one X chromosome regulates the quantitative conditions in favour of femaleness, the presence of two X chromosomes in the direction of maleness. The opposite is the case for male heterozygotism with the formula (M) Ff = ♂ and (M)FF ♀; here one X chromosome favours maleness and two X chromosomes female development. Now it follows from this that if parthenogenesis leads to the development of only one sex, some mechanism must be responsible for the right combination of the X chromosomes. What happens with the other chromosomes is not relevant. Whether the normal or the reduced chromosome number is present in parthenogenetic eggs is only of significance in so far as the presence of one or two X chromosomes is concerned. It is well to be completely clear about this, since otherwise a hopeless confusion will result, for there are parthenogenetic eggs which give females without reduction, others which give females after reduction, some again which give males with reduction, and others which give both sexes with and without reduction, etc.

From this point of view let us glance over the most important facts.

1. Parthenogenesis as a Medium for the Normal Distribution of the Sexes

The Hymenoptera, the bees in particular, provide us with the classic example of parthenogenesis participating in the mechanism of the production of the sexes. The fundamental fact which is a matter of general knowledge is that bee eggs developing parthenogenetically only give rise (normally) to males (the drones), whilst fertilized eggs develop into females, the workers and queens. This so-called theory of Dzierzon is now, after endless discussion, firmly established. The biological basis is provided by the fact that unfertilized queens, or old queens whose sperm supply in the receptaculum is exhausted, are only able to produce drones.

Only one breeding experiment can be brought forward which is altogether free from objection—that of Newell.[1] The difficulty of the experiments consists naturally in the fact that the fertilization of the queen takes place during the nuptial flight, that is, it is uncontrolled. Consequently an experiment is only free from objection when all drones other than those of the experiment can be regarded as excluded. The investigation can only be carried out in a completely isolated locality. Newell was able to do this in Texas. He crossed the yellow Italian bees with the grey Cariolarian. The cross Italian queen × Cariolarian males gave nothing but yellow F_1 animals. Yellowness is therefore dominant over grey colour in the héterozygote females. The males must naturally all be yellow if they are produced parthenogenetically. The reciprocal cross Cariolarian queen × Italian males gave yellow workers and grey drones, and this also corresponds to the expected. Finally, the hybrid females gave both yellow and grey drones. It is clear, therefore, without further discussion that the results are exactly what is to be expected on the theory of Dzierzon.

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[1] Newell, W., "Inheritance in the Honey Bee." Science, 41, 1914.

The mechanism of this kind of sex differentiation is also known now, in particular through the work of Petrunkewitsch, Meves, and Nachtsheim.[1] The normal chromosome number of the bee queen is thirty-two. A sex chromosome is present, but morphologically is indistinguishable from the others. Maturation divisions take place in each egg, reducing the chromosome number to sixteen. If now such an egg is fertilized it develops into a female. Assuming that one of the paternal chromosomes is an X chromosome, a fertilized egg will therefore contain two X chromosomes and the case can be represented by the formula (M)FF = ♀. If the egg is not fertilized, it develops into a male. This development takes place, however, with the reduced number of chromosomes—that is, with only one X chromosome, and the formula corresponding would be (M)F = ♂.

Meves has discovered that in the spermatogenesis of these male bees no reduction division takes place, only an apparent division without participation of the chromosomes (see Fig. 100). All the sperm cells are therefore of one kind, that is, with sixteen chromosomes, and so the cycle is completed.

It will be clear that the facts fit completely into the scheme of the sex mechanism already made known, the special feature of the case being only that the bees do not employ the usual method of heterogametism for the establishment of the sex ratio, but attain the same result in regard to the quantitative combination of the sex enzymes by the employment of parthenogenesis with homogametism in both sexes.

From the standpoint of the theory of sex inheritance these discoveries are of far-reaching general significance. The identity of the Mendelian interpretation and the cytological facts in regard to the sex chromosomes was deduced on the basis of heterogametism – homogametism = heterozygotism – homozygotism. If, however, we would express the case of the bees in Mendelian symbolism, we encounter serious difficulties. Both sexes are homogametic and thus produce only one kind of germ cells. For the Mendelian scheme we require heterogametism. On the other hand, the male is heterozygotic since it has only one sex factor, yet notwithstanding this it produces only one kind of gamete. The position suffices to show that in using the Mendelian symbolism one must be quite clear as to what it indicates. It only has a meaning when brought into relation on the one hand with the cellular mechanism, and on the other with definite physiological concepts.

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[1] Petrunkewitsch, A., "Die Richtungskörper und ihr Schicksal im befruchteten und unbefruchteten Bienenei." Zool. Jahrb., 14, 1901.—Meves, F., "Die Spermatocytenteilungen bei der Honigbiene usw." Arch. mikr. An., 71, 1907.—Nachtsheim, H., "Cytologische Studien über die Geschlechtsbestimmung bei der Honigbiene." Arch. Zellf., 11, 1913.

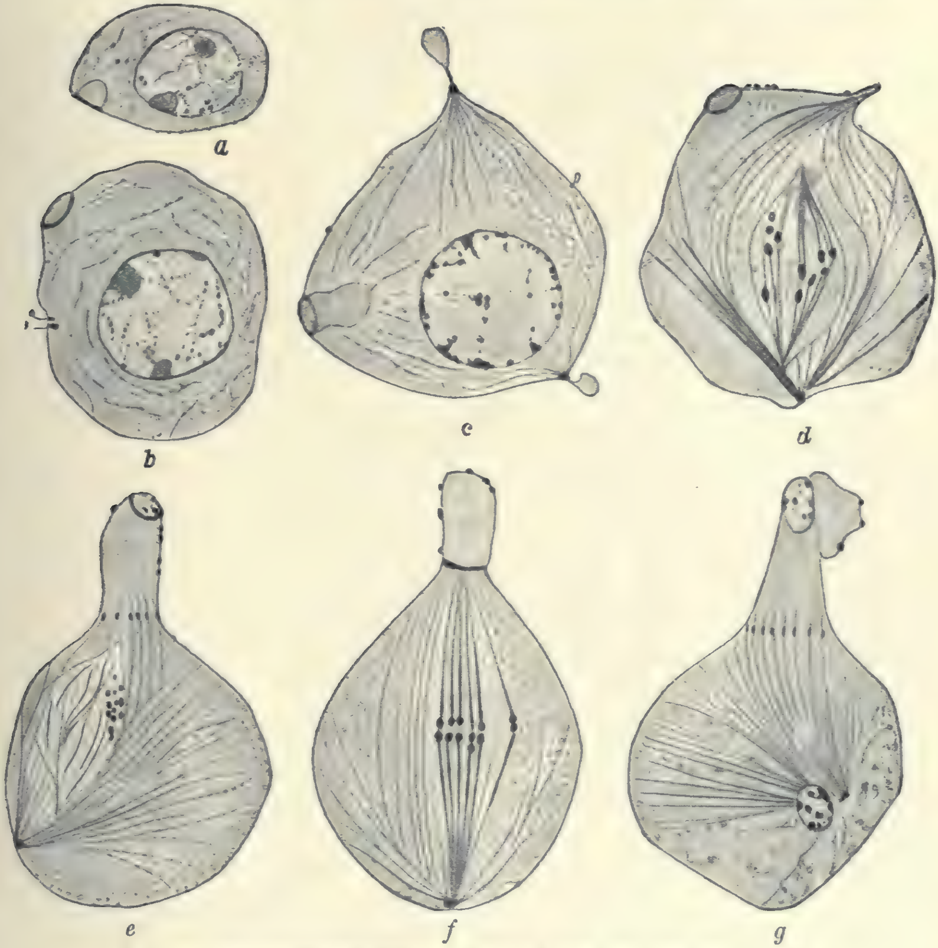

FIG. 100.—The abortive maturation spindle of the drone bee spermatocyte.
After Meves from Buchner.

The case of the bee, so far as we have followed it, is quite clear in regard to the mechanism of inheritance. It is necessary, however, to point out that behind this there is still a great biological problem. The mechanism described above stands, in so far as it differs from the conditions found almost everywhere else in the animal kingdom, as a peculiarity which is perhaps a necessary condition for the phylogenetic development of the bee and ant societies. The normal mechanism of sex distribution in the animal kingdom leaves the whole thing in the hands of chance, but the interpolation of parthenogenesis into the mechanism renders it possible for the mother bee, one might say, to control the sex. That this is actually practised, and that the anatomical means are present in the so-called sperm-pump, is generally known (see Breslau,[1] Adam,[2] and Fabre[3]). But it was only the control of sex which rendered possible the development of the biological conditions of these insect states with their sterile workers, only once fertilized queen, and the transitory occurrence of males, etc. The peculiarity of the mechanism was certainly the primary development, for it has also found a use in other groups and under other biological conditions.

The above does not suffice, after all, to settle the question of the relationship of parthenogenesis to sex in the bee. It was stated above that *normally* the processes of sex inheritance followed the theory of Dzierzon. Putting it this way left the possibility that something else took place in exceptional cases. As a matter of fact there is a problem which is usually, and mistakenly, disavowed but which crops up again and again. There are bee-keepers who believe that under certain conditions drones may be obtained from fertilized eggs. The value of the assertion has often been discredited by its own champions through absurd attacks having been made on elementary biological facts. We must not allow ourselves to be influenced by this, and hesitate to prove the statement, or be led into denying *a priori* its possibility—particularly to-day when we possess the knowledge to explain it in case the occurrence should turn out to be correct.

The investigations now to be considered have been carried out by Dickel senior and junior, Breslau, Heck, Petillot, and others.[1] Essentially they all run on the following lines. From a hive in which there are exclusively worker cells with young brood the queen is removed and the hive closed. After a period, and in fact such a short period that only the worker larvæ present can come into consideration, drone brood are found in the hive and drones emerge. According to Dickel junior the bee-keeper Petillot combined this experiment with the use of different races, the gold-yellow American and the black German races. He killed all the drone larvæ in a hive of the black race ripe for swarming, and then carried over worker larvæ of the yellow race into young drone cells of the black hive. "In three to four weeks the black folk shimmered with beautiful gold-yellow drones." If this experiment is free from objection, it indicates that drones can be produced from fertilized eggs. Experience teaches us, it is true, that one must be sceptical regarding breeders' notes, for they are usually not altogether clear about the conditions necessary for an exact experiment. Nevertheless it is remarkable how frequently the same statements occur, and Breslau, who carried out an exact verification, had a positive success at least once. In addition we have the communications of such distinguished observers as Pérez and Cuénot, who found a few scattered drones with yellow colour amidst the black ones in hybrid stocks of yellow and black races. The possibility of the production of drones from fertilized eggs must therefore not be lost sight of.

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[1] Breslau, E., "Der Samenblasengang der Bienenkönigin." Zool. Anz., 29, 1905.

[2] Adam, A., "Bau und Mechanismus des Receptaculum seminis bei den Bienen, Wespen, und Ameisen." Zool. Jahrb., 35, 1901.

[3] Fabre, J. H., "Souvenirs entomologiques." Paris, 1890, 3 Sér.

Let it be supposed that the above had actually been demonstrated. What would be its significance? On a previous page, when discussing the chemical side of the sex problem, reference was made to the form-determining influence of the food of the bee larvæ; the workers could produce at will a worker or a queen bee from a fertilized egg. The means can only be the food, whether it be owing to its general chemical composition or through some special secretion product of the workers as yet unknown. As a matter of fact the chemical constitution of the food is very different indeed, as the following table of Planta[1] shows after (Straus).

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[1] Dickel, O., "Zur Geschlechtsbestimmungsfrage bei den Hymenopteren." Biol. Centrbl., 34, 1914.—Breslau, E., "Über die Versuche zur Geschlechtsbestimmung der Honigbiene," etc. Zool. Anz., 33, 1908. (See also the criticisms of these experiments by Nachtsheim, Biol. Centrbl., 94, 1914.)—Cuénot, L., "Les mâles d'abeille proviennent—ils toujours d'œufs parthénogénétiques?" Bull. Sc. France-Belgique, 43, 1909.

COMPOSITION OF THE FOOD OF BEES

	Queen food	Drone food.			Worker food.		
	Average.	Less than 4 days.	Over 4 days.	Average.	Less than 4 days.	Over 4 days.	Average.
Proteid . .	45·14	55·91	31·67	43·79	53·38	27·87	40·62
Fat . . .	13·55	11·90	4·74	8·32	8·38	3·69	6·03
Glucose . .	20·39	9·57	38·49	24·03	18·09	44·93	31·51

We are now reminded of the sexuality conditions of *Boneliia* already described, where the secretion of the proboscis determines whether a larva will be a male or not. We are reminded too of our discussion on zygotic and hormonic intersexuality and of the transformation of germ plasm which should be female-determining into male-determining. In the light of the facts referred to, it would not be altogether surprising if the bee workers had an analogous power, namely, that of increasing the velocity of reaction of the male enzyme, or what is more probable, in view of the case of *Crepidula plana*, of disturbing the velocity of differentiation of the organs, or even of altering directly the chemical reactions of the body (by means of the special nature of the food) and thus bringing forth male bees out of fertilized and therefore female eggs; in short, in the same way as male Gipsy moths were obtained from female-determined eggs owing to abnormal quantitative combinations of the sex enzymes. Demonstrated it is not—but there are no grounds for doubting the possibility *a priori*.

The employment of parthenogenesis as a sex-determining agent is thus physiologically and genetically quite intelligible. And there is no reason to doubt that cases not yet completely investigated will fit in with the same kind of explanation. The sex-determining mechanisms at the disposal of parthenogenesis may be employed or combined in the most diverse manner: parthenogenesis with and without reduction and with male or female heterozygotism, combined with fertilization by two kinds of spermatozoa or only one, will suffice to explain all cases.

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[1] Planta, "Der Futterbrei der Bienen." Ztschr. phys. Chem., 12, 13, 1888-89.

When, for example, Reichenbach and Crawley state[1] that occasionally unfertilized ant workers gave rise to female progeny we can assume, until evidence to the contrary is forthcoming, that some cause has resulted in the falling out of the reduction division (see later discussion on the question of influencing the course of the maturation divisions). When we are told that the workers of the Cape Honey Bee[2] can easily be influenced to reproduce parthenogenetically whereby they produce chiefly workers and queens (that is to say, females), so it is to be expected that parthenogenesis is here unaccompanied by chromosome reduction. Again, when it is stated that *Aleurodes vaporariorum*[3] produces only females parthenogenetically in many localities whilst only males result in other districts, but that the same females fertilized give both sexes, we may justly expect that parthenogenesis occurs here both with and without reduction, together with fertilization combined with male digametism.

Finally, another possibility still exists for the exceptional appearance of females from parthenogenetic eggs and of males from fertilized bee and ant eggs. The reader is reminded of the studies of Bridges on the non-disjunction of the sex chromosomes during the maturation division (see p. 71). If such an abnormality occurs amongst the Hymenoptera, it would be possible for ripe eggs to be produced containing two X chromosomes as well as ripe eggs with none. The first would give females parthenogenetically whilst the latter would, after fertilization, give males. If both these occurrences took place regularly in a definite percentage of cases in a hive, one would have reason to assume non-disjunction as the cause.

2. Parthenogenesis and Cyclical Sexuality

In the cases belonging to this group parthenogenesis does not replace the homoheterogametic mechanism as in the bee, but works together with it within a system of cyclical sexuality.

The example best known cytologically is the Aphidæ, but this has already been discussed (see p. 57 and Fig. 37 for details). It may be pointed out again that in this case, where females arise parthenogenetically, the two X chromosomes remain in the egg through the falling out of the maturation division, and that the parthenogenetic production of males is rendered possible through the removal in a special manner of one X chromosome during polar body formation without reduction. Furthermore, the fertilized eggs give nothing but females, because the male-determining spermatozoa without X chromosomes fail to live.

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[1] Reicherbach, H., "Über Parthenogenese bei Ameisen usw." Biologisches Centrbl., 22, 1912.—Crawley, W. C., "Parthenogenesis in Worker Ants," etc. Trans. Entomol. Soc., London, 1911.

[2] Jack, R. W., "Parthenogenesis amongst the Workers of the Cape Honey Bee." Mr. G. W. Onion's Experiments. Trans. Entomol. Soc. London, 1916.

[3] Williams, C. R., "Some Problems of Sex Ratios and Parthenogenesis." Journ. of Genetics, 6, 1917.

From the standpoint of the mechanism of sex distribution this case is therefore quite clear. The conditions are presumably the same in the Daphnids, but the cytological details are not yet satisfactorily known.

The cyclical type of reproduction can also be combined with sexual conditions resembling those of the bee, and this is the case amongst Rotifera and certain Hymenoptera. In the first-named group the mechanism of sex determination is in principle of the same constitution as that of the bees and ants: one X chromosome determines a male and two X chromosomes a female.

In the formation of the parthenogenetic summer eggs only one polar body is formed (see Erlanger and Lauterborn[1]) and the chromosome number is not reduced (Whitney[2]). All the progeny are females. In the formation of males and resting eggs chromosome reduction takes place; if the eggs are unfertilized they give males, if fertilized they develop into females, as in the bee. The reason why all fertilized eggs give females lies in the fact that half the spermatozoa (analogous to the case of the Aphids) are incapable of functioning (Whitney).

The gall wasp, *Neuroterus lenticularis*, studied by Doncaster,[3] also belongs to this category. Females only arise from fertilized eggs, for, as in the bees, only one kind of spermatozoon is formed. These females reproduce parthenogenetically, and produce either females out of non-reduced eggs (chromosome number twenty) or males out of reduced eggs (ten chromosomes). According to Armbruster[1] primitive bees of the genus Halictus conduct themselves in a similar manner, which is very significant so far as the relation of sex-determining parthenogenesis to the phylogeny of the bee state is concerned (see above). In regard then to the sex distribution mechanism all these cases are quite clear. Other problems which they present will soon occupy our attention.

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[1] v. Erlanger, R., and Lauterborn, R., "Über die ersten Entwicklungsvorgänge im parthenogenetischen und befruchteten Radertierei." Zool. Anz., 20, 1897.

[2] Whitney, D D., "Observations on the Maturation Stages of Parthenogenetic and Sexual Eggs of *Hydatina senta*." Journ. Exp. Zool., 6, 1909.—"The Production of Functional and Rudimentary Spermatozoa in Rotifers." Biol. Bull., 33, 1917.

[3] Doncaster, L., "Gametogenesis of the Gall-fly *Neuroterus lenticularis* (*Spathegaster baccarum*)." Proc. R. Soc. London, 82, 83, 1910.

3. Parthenogenesis as a Rudimentary Condition of Bisexuality

Under this heading we shall consider such cases in which the bisexuality is completely or almost completely repressed, and females alone are present which continue always or almost always to produce females parthenogenetically. These cases are not altogether rare amongst Nematodes, Insects, and Crustacea. One's attention is again drawn above all to the sex distribution mechanism, and it can be said that where exact information is available regarding this the facts agree with the foregoing—that is, no reduction of the chromosomes takes place, so that the females arising from the parthenogenetic eggs always have the same hereditary constitution as their mothers. Under these conditions it is naturally all the same in the end which sex is the heterozygote.

So far as details are concerned this parthenogenesis without reduction takes place in different ways—three chief types being known. The first type is that which occurs in the parthenogenetic species of Ostracods like *Cypris reptans* and *fuscata.* Weismann and Ischikawa showed some time ago that the parthenogenetic eggs of these species only formed one polar body, and Woltereck and Schleip[2] demonstrated that no reduction division took place and development followed with the complete chromosome number.

The second type (Fig. 101), which gives the same final result, is found in some of the parthenogenetic *Artemia* (some of these conduct themselves like the previously mentioned type), where it was discovered by Brauer.[1] It is the well-known fertilization by the polar body nucleus. After the maturation division the nucleus of the polar body migrates again towards the egg nucleus and fuses with it so that the old conditions are restored (Fig. 101). The accuracy of this description has often (and unjustly) been doubted (Petrunkewitsch, Artom[2]). The phenomenon is, however, not an isolated one since O. Hertwig and Buchner[3] have described exactly

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[1] Armbruster, L., "Zur Phylogenie der Geschlechtsbestimmungsweise bei Bienen." Zool. Jahrb., 40, 1916.

[2] Weismann, A., and Ischikawa, C., "Weitere Untersuchungen zum Zahlengesetz der Richtungskörper." Zool. Jahrb. (An.), 3, 1889.—Woltereck, R., "Zur Bildung und Entwicklung des Ostracodeneis." Z. wiss. Zool., 64, 1898.—Schleip, W., "Vergleichende Untersuchung der Eireifung usw." Arch. Zellf., 2, 1909.

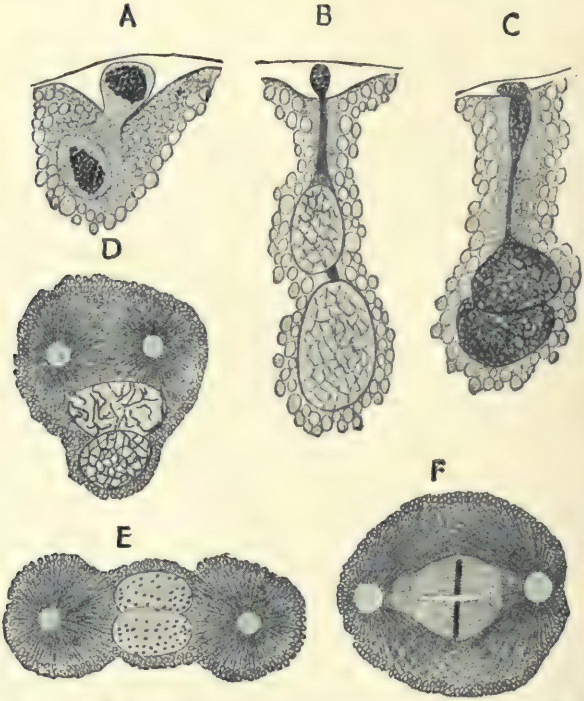

Fig. 101.—Six stages of the polar body formation and conjugation of the polar body nucleus with the egg nucleus in the parthenogenetic *Artemia*.

After Brauer from Korschelt-Heider.

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[1] Brauer, A., "Zur Kenntnis der Reifung des Eies der parthenogenetisch sich entwickelnden *Artemia salina*." Arch. mikr. An., 43, 1894.—Petrunkewitsch, A., "Die Reifung der parthenogenetischen Eier von *Artemia salina*." Zool. Anz., 21, 1902.—Artom, C., "Analisa comparativa della sostanza cromatica," etc., Arch. Zellf., 7, 1911.

[2] See previous footnote.

[3] Buchner, P., "Die Reifung des Seesterneis bei experimenteller Parthenogenese." Arch. Zellf., 6, 1911.

the same kind of thing in the artificial parthenogenesis of the starfish egg.

The third type has been described by Doncaster[1] for the Tenthredinid *Nematus* and by Schleip[2] for the gall wasp *Rhodites rosæ*. In this type there is no synaptic union of the chromosomes so that the normal number takes part in the maturation divisions. Two maturation divisions occur, but both are equational divisions and no reduction of the chromosome number occurs. The development is completed, therefore, with the unreduced number of chromosomes, although outwardly the polar body formation appears quite normal.

All these cases are then quite clear in regard to the sex-determining mechanism so far as the production of parthenogenetic females is concerned. In many of these forms, however, males are also occasionally produced parthenogenetically. There are, for example, almost pure female races of *Artemia* and others more or less rich in males. The same holds good for the fresh water Phyllopods, and also for the Phasmids so far as is known. In regard to the cytology of these processes we are still without information, but we can predict with confidence that it will bring no surprises.

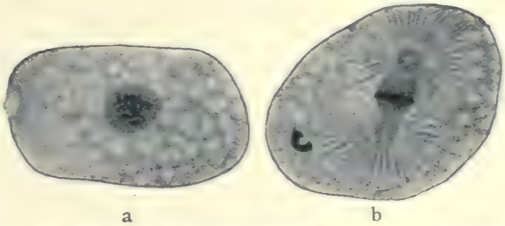

FIG. 102.—The fertilization of *Rhabditis aberrans*: a, penetration of the spermatozoon; b, first segmentation stage with the sperm nucleus lying to one side. After E. Krüger.

Amongst the Nematodes there are also many parthenogenetic species, as Bütschli[3] discovered years ago. Their cytology is unknown. On the other hand, Krüger[4] has given us some information in regard to a very peculiar parthenogenesis in a free living *Rhabditis* with which we have already become acquainted in another connection. Here it is true a spermatozoon penetrates the egg, but it dies there and the egg itself develops parthenogenetically into a female without any reduction. The sperms themselves are only of one kind—female-determining—and only exceptionally through the loss of a chromosome does a male-determining sperm result. It appears that such a sperm is capable of fertilization, and that in this case as a rare exception a male is produced. Fig. 102 depicts some of the chromosome conditions of this worm.

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[1] Doncaster, L., "On the Maturation of the Unfertilized Egg," etc. Qu. Journ. Mic. Sc., 49, 1906.

[2] Schleip, W., "Die Reifung des Eis von *Rhodites rosæ* usw." Zool. Anz., 35.

[3] Bütschli, O., "Beiträge zur Kenntnis der freilebenden Nematoden." Nova Acta Leop., 36, 1875.

[4] Krüger, E., "Die phylogenetische Entwicklung der Keimzellenbildung einer freilebenden *Rhabditis*." Zool. Anz., 40, 1912.

4. Accidental Parthenogenesis

Accidental parthenogenesis is the occasional occurrence of parthenogenesis in otherwise normally sexual forms. Authentic cases of this kind are known for the silk worm moth *Bombyx mori*, and the Gipsy moth *Lymantria dispar.* In both cases the parthenogenetic eggs develop into both sexes and in normal numbers. The cytological changes during maturation are not known, but it has been possible to determine that the parthenogenetically produced caterpillars possess the normal number of chromosomes.[1] Without a knowledge of the cytology of the maturation divisions it is naturally impossible to say whether the processes taking place are in agreement with the above views on the mechanism of sex distribution. Since the female is certainly heterozygotic in this case, a fact which does not apply to all of the examples mentioned in the foregoing pages, these moth cases might provide a test.

5. Artificial Parthenogenesis

The investigation into artificial parthenogenesis may also add an iota to this chapter, although up to date the knowledge gained is still rather small in amount. The only cases in which the sex of the parthenogenetically produced individuals, as well as their cytology, is known are the sea urchin and the frog. Numerous investigations have shown that the parthenogenetic sea urchin larvæ develop with the reduced number of chromosomes, and further that the male sex is the digametic one. The few individuals which Delage[2] was able to rear turned out to be males, which corresponds with the expectations. Only in one case have artificially parthenogenetic animals been reared up to sexual maturity—namely, J. Loeb's frogs,[1] and up to date this worker has found mostly males, although also a number of females.

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[1] Goldschmidt, R., "On a Case of Facultative Parthenogenesis in the Gipsy Moth," etc. Biol. Bull., 1917.

[2] Delage, Y., "Le Sexe chez les oursins," etc. C.R. Ac. Sc., Paris, 148, 1910.

We had the opportunity of investigating these male frogs cytologically and found that a perfectly normal spermatogenesis took place with the non-reduced chromosome number[1] (2n = 26), the same figure which Brachet found as the normal chromosome number in the tissue cells of parthenogenetic frog larvæ. Fig. 103 is an illustration of the chromosomes of a spermatogonium of this frog. The chromosome number must, therefore, in some way have again been restored.

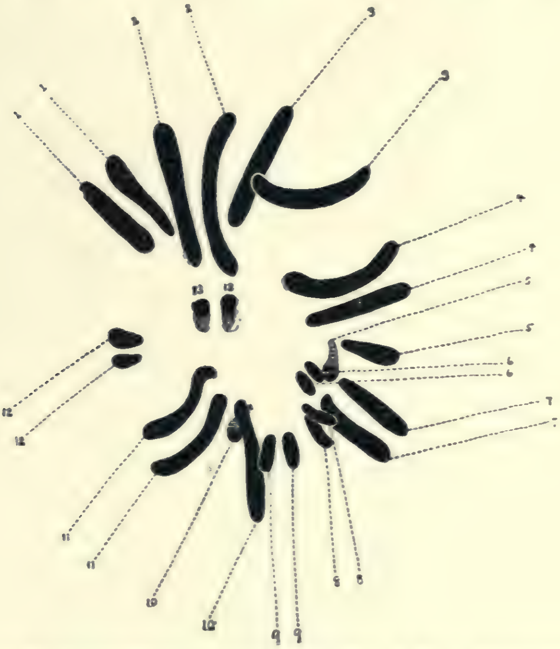

Fig. 103.—The twenty-six chromosomes (thirteen pair) of the spermatogonium of an artificially-parthenogenetic frog.

Different workers, Levy, Hertwig, Parmenter, and Hovasse,[3] have in the main brought forward the same discoveries regarding this subject. It appears that in the regulation of the chromosome number all sorts of numbers from the haploid to the diploid condition may occur. But only the diploid individuals are capable of existence. It is impossible to say at present what are the relations to sex here. The solution is particularly difficult owing to the many peculiarities in connection with sex determination in frogs.

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[1] Loeb, J., "The Sex of Parthenogenetic Frogs." Proc. Nat. Ac. Sc., Washington, 2, 1916.

[2] Brachet, J., "Etudes sur les localizations germinales," etc. Arch. Biol., 27, 1911.—Goldschmidt, R., "Kleine Beobachtungen und Ideen zur Zellenlehre, II." Arch. Zellf., 15, 1920.

[3] Levy, F., "Die Kernverhältnisse bei parthenogenetischen Fröschen." Sitzber. d Preuss. Akad. d. Wiss., 24, 1920.—Hertwig, G. und P., "Triploide Froschlarven."

There can also be no doubt that in other species artificial parthenogenesis leads to cellular conditions which are not the same as those in the sea urchin. Buchner found (l.c.) that in the starfish the restoration of the normal number of chromosomes was brought about through copulation of the polar body nucleus with the egg nucleus. Another type of restoration of the normal number of chromosomes was described by Kostanecki in *Mactra*.[1] In this case after the reduction the chromosomes split but no division occurs. One may call it a rudimentary division. Its effect is the duplication of the chromosome number, i.e. the restoration of the unreduced number which is then found in all the following divisions. Further facts are to be awaited.

6. Conclusions

It may be asserted with justification that in so far as the relation of parthenogenesis to sex is concerned, the explanation of the cytological mechanism of sex distribution and its quantitative-physiological significance has proved illuminating. Without this it would have been scarcely possible to understand the apparent diversity of the phenomena. As a matter of fact it is also here that all the old theories of sex are wrecked. It may, in conclusion, not be unreasonable therefore to state once again the different possibilities allowed by the chromosome mechanism in the relation of parthenogenesis and sex.

Arch. mikr. Anat. Festschr. f. O. Hertwig, 1920.—Parmenter, C. L., "The Chromosomes of Parthenogenetic Frogs." Journal General Phys., 2, 1920.—Hovasse, R., "Contribution a l'étude des chromosomes." Bull. Biol., France-Belgique, 1922.

[1] Kostanecki, K., "Cytologische Untersuchungen an kunstlich parthenogenetisch sich entwickelnden Eiern von *Mactra*." Arch. mikr. An., 64, 1914.

1. *Female Heterozygotism*

One X chromosome (= factor M) = ♀
Two X chromosomes (= factors MM) = ♂

A. Parthenogenesis with reduced chromosome number.

All the progeny must be female since XX (= MM) cannot occur.

B. Parthenogenesis with non-reduced chromosome number.

All the progeny must be female, since the maternal conditions remain unaltered.

(*a*) Where the non-reduced chromosome number arises through a process such as that in *Mactra*, that is, rudimentary fission after reduction, both sexes can arise, namely, MM and mm, assuming that the mm eggs (those without X chromosomes at all) are capable of development.

2. *Male Heterozygotism*

One X chromosome (= factor F) = ♂
Two X chromosomes (= factors FF) =

A. Parthenogenesis with reduced chromosome number.

All the progeny are male. Only the occurrence of "non-disjunction" (both X chromosomes remain in the egg) could exceptionally give females.

B. Parthenogenesis with non-reduced chromosome number.

All the offspring are females. But if an X chromosome is lost during the formation of a polar body without reduction, as in the Aphids, males will result.

(*a*) When, as above, the conditions of the *Mactra* type are present, all the progeny is similarly FF thus female.

C. The combination of these types in the same object will give every conceivable result.

B. Parthenogenesis as a Means to Cyclical Sexuality

The knowledge of the mechanism which controls the resulting sex in parthenogenetic reproduction does not imply a complete understanding of the relations of parthenogenesis to sex. When an Aphid egg, for example, develops now with, and now without, reduction, whilst other eggs lose an X chromosome without reduction, these are departures from the type of the mechanism which must have a cause.

Now if species which present these conditions are more closely observed, it will be seen that they are characterized by the biological phenomenon of cyclical sexuality. The occurrence of the different varieties of the mechanism is not irregular, but is in the closest association with the whole life history of the species and this runs in definite cycles. Such a cycle in the Aphids, setting aside endless variations in details, runs in principle as follows :—

A fertilized egg, characterized by special biological features, rests through the winter and out of it in the springtime a female hatches which initiates the summer generation of females by parthenogenetic reproduction. These females in their turn reproduce in a similar manner. Finally sexuiparous females appear which are morphologically different from the others and these produce parthenogenetically males and females.

These sexuiparous females are generally of two kinds, male producers and female producers, and they only produce one definite sex from their parthenogenetic eggs. The fertilized eggs which result from this generation are then the winter eggs. This life history clearly indicates the existence of a close connection between the sexual cycle and the outer conditions in the course of the different generations, and herein lies the possibility of investigating experimentally the causes which set the mechanism into action.

Now the different varieties of the mechanism consist in specificities of the maturation divisions of the egg, together with the ability to develop parthenogenetically or not, and so the chief problem resolves itself finally into the discovery of the factors which can influence the maturation divisions and parthenogenesis. It will be of advantage to glance first at analogous possibilities where there is no cyclical sexuality.

1. The Possibility of a Directing Influence in the Maturation Division Mechanism in Cases of Normal Sexuality

In normal bisexuality one is naturally only concerned with influences which, acting on the mechanism of maturation division of the egg, exert a directional influence on the mitosis instead of leaving it a matter of chance. For example, in the presence of female heterozygotism such an influence could determine either that only X eggs or Y eggs were formed, the first giving only males, the latter only females. With male heterozygotism the postulated influence could act somewhat like the non-disjunction in *Drosophila* causing either both X chromosomes to pass into the polar body, so that only males could be produced, or to keep both back in the egg, resulting exclusively in female development. Up to quite recently the only facts available made the occurrence of such phenomena seem rather probable. First and foremost there are the experiments carried out originally by Pfluger and discovered independently by Richard Hertwig and confirmed by Kuschakewitsch (loc. cit.), giving the same results in all cases. When frog eggs were artificially brought into an over-ripe condition, as a result of actual separation of the mating pairs, they produced 100 per cent males. Since the experiments have been repeated many times with the exclusion of all sources of error and always with the same result, no doubt can arise as to their accuracy. Different authors have tried different explanations; one was most inclined to assume that chemical alterations in the egg connected with the over-ripeness had exercised a directional influence on the maturation divisions. This was the assumption of Richard Hertwig. In the meantime it has been found that this assumption which sounds so probable is wrong. In the first place Crew and Witschi, as mentioned earlier in this work, have shown that the male sex is heterogametic in the frog. Then R. Hertwig[1] has been able to show the probability that in such an experiment half the individuals begin their development as females and then only are transformed into males. This example must therefore be excluded.

In the same category one might place the conditions which exist, according to Whitman and Riddle[2] in pigeons. At the same time it must be noted that the facts themselves are neither clear nor convincing. It is an often discussed problem that, of the two eggs which pigeons generally lay one after the other, the first gives a male and the second a female. Although constantly shown to be incorrect (Cuénot and Cole),[3] Riddle and Whitman state that it is actually a fact if one uses pure species, though exceptions may occur. Now Riddle finds that typically the first egg is smaller and contains less chemical energy than the second. Thus, according to him, there is a visible dimorphism of the egg which is associated with the sex. Since in the pigeons the female is heterogametic, one could take this as indicating that the chemical differences of the eggs exercised a directional influence on the maturation division; the chemical investigations of Riddle would then enable us to obtain a glimpse into the conditions of such an influence.

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[1] Hertwig, R., "Über den Einfluss der Ueberreife der Eier auf das Geschlechtsverhältnis von Fröschen und Schmetterlingen." Sitz. Ber. Bayr. Akad. d. Wiss., 1921.

[2] Riddle, O., "Sex Control and Known Correlations in Pigeons." Amer. Nat., 50, 1916.—"The Control of the Sex-ratio." Journ. Washington Ac. Sc., VII., 1917.

[3] Cuénot, L., "Sur la détermination du sexe chez les animaux." Bull. Sc., France-Belgique, 32, 1899.

Riddle, however, does not accept this point of view and for the following reason. When the particular pigeons which present these conditions of the sexes are crossed with other genera, one finds that at the beginning of the breeding season almost only males are produced, at the end almost only females. If, however, an abundant egg production is forced, the tendency to produce nothing but female progeny occurs earlier. Hybridization or overwork is said, therefore, to have this curious sex changing influence, which in his opinion is cytologically inconceivable. The point is that Riddle at the same time takes it as quite clear that in these cases also the first egg is male and the second really female-determining, notwithstanding which two similar sexes arise. As further evidence against the cytological explanation he adds that the eggs from such crosses also give intersexual animals.

But there is no kind of evidence for this, since the individuals denoted as intersexes are perfectly normal in structure and are fertile females. According to Riddle they behave like males when they are isolated with other females. Since this is as common with pigeons as with many other animals there is no ground for regarding these birds as being other than normal females.

It is very difficult to form an idea of the phenomena we have to deal with from the publications of Riddle up to date. It is quite possible that a mixture of two quite different phenomena is concerned, one of which is the directional influence of the chemical constitution of the egg on the maturation divisions, the other a change of sex resulting from the crossing of far removed genera. Finally, one could regard the generic crosses as a kind of indirect parthenogenesis, as is the case with certain Amphibian hybrids. All in all it appears as if we shall have to wait a little before passing a judgment on this case.

Fortunately Seiler[1] has succeeded in obtaining evidence, by direct experiment, that an influence on the direction of the maturation divisions in regard to the X chromosome mechanism is possible. The evidence can naturally only be obtained with animals where female heterozygotism is the rule. We mentioned on a previous page (p. 57) the exceptionally clear X chromosome conditions which exist in the eggs of the Psychid *Talæporia tubulosa.* By counting the maturation spindles in the eggs Seiler was able to determine that the ratio of the eggs in which the X chromosome goes into the polar body to those in which it remains in the eggs (male-determining) was exactly the same as the natural proportion of ♂ and ♀. Since the moment at which the distribution of the X chromosomes in the maturation divisions takes place was exactly known, an attempt was made experimentally to influence the direction of the maturation divisions at the right time. The work was successful both with the employment of different temperatures as well as with over-ripeness. The following table gives the clear result as obtained from the direct enumeration of the chromosome conditions:—

Origin of the Material.	Experimental Action.	No. of Cases in which X Chromosomes Wandered		♀ : ♂
		Outwards.	Inwards.	
Tornow . .	Eggs laid at room temp. about 18° C.	61	45	136 : 100
Liegnitz & Tornow	35-37° C. during the maturation division.	52	84	62 : 100
,, ,,	3-5° C. during the maturation division.	48	31	155 : 100
,, ,,	Intra-uterine over-ripeness up to 4 days.	104	145	72 : 100

With this research the possibility of the action of directing influences on the maturation division is demonstrated (see also later in reference to the ratios of the sexes).

This is now the place to refer further to the visible sexual dimorphism of certain eggs. The only case free from objection is the little worm *Dinophilus*, in connection with which Korschelt

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Seiler, J., "Geschlechtschromosomenuntersuchungen an Psychiden." Arch. Zellf., 15, 1920.

discovered that each of its broods contained small male eggs and large female eggs. This gives us naturally a complicated situation for the mechanism of sex distribution. Male heterozygotism does not come into the case at all, for the eggs are already sexually determined. The assumption of female heterozygotism hits up against the difficulty that the eggs are determined long before the maturation divisions. Unfortunately the attempts made so far to explain the case have failed. One of the peculiarities of *Dinophilus* is that the eggs are fertilized before the oocyte growth takes place (Shearer, Nachtsheim[1]). One might suppose, therefore, that heterogametic sperms exercised an influence on the visible differences of the eggs. De Beauchamp[2] and Nachtsheim showed, however, that parthenogenetic eggs were likewise sexually dimorphic. Another possibility is that, like the eggs of Rotifera, the male eggs develop parthenogenetically haploid. But they show the normal course of fertilization (Nachtsheim).

Since now into the bargain no X chromosomes are to be demonstrated, there seems no possible way of explaining the case other than the following: The female is heterozygotic and possesses, as in so many other cases, a non-distinguishable XY-group. Unknown active factors present in the egg plasma (which have been termed controlling factors)[3] so condition things that in the eggs which store up the greatest quantity of yolk (female eggs) the maturation divisions are compelled to run so that the X chromosome goes into the polar body, the converse being the case in the male eggs. As it is known that there are such controlling factors which, in addition to influencing the course of the maturation divisions (reduction-non-reduction in Daphnids), determine in the same eggs the protoplasmic differences (summer and winter eggs of Daphnids), the above solution seems at present to be the one which falls in best with the known phenomena.

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[1] Shearer, C., "The Problem of Sex-Determination in *Dinophilus gyrociliatus*." Qu. Journ. Micr. Sc., 57, 1912.—Nachtsheim, H., "Das Problem der Geschlechtsbestimmung bei *Dinophilus*." Ber. Nalf. Ges. Freiburg, 21, 1914.—"Cytologische und experimentelle Untersuchungen usw." Arch. mikr. An., 93, 1919.

[2] Beauchamp, P. de, "Sur l'existence et les conditions de la parthénogènèse chez *Dinophilus*." C.R. Ac., 150, 1910; further see *ibid.*, 154, 1912.

[3] Correns-Goldschmidt, "Vererbung und Bestimmung des Geschlechts." Berlin, 1913.

2. Cyclical Sexuality

As has already been stated in a preliminary way, the problem of cyclical sexuality is to explain the causes which act in a typical directional manner on the mechanism of sex distribution. This cannot be sufficiently emphasized as against the assumption that this cyclical sexuality permits of conclusions being drawn regarding the physiology of sex determination. If the facts are not merely regarded as isolated data, but are brought into conjunction with our knowledge of the mechanism and physiology of sex determination as a whole, there can be no doubt that parthenogenesis and sexuality in the cyclical forms—apart from their biological significance—are only methods of regulation of the mechanism of sex distribution, not very different from those, for example, in the bee. That the details of the mechanism are still incompletely understood is no objection, for they are sufficiently known to enable us to classify them with the rest of our information.

It is known that in the Rotatoria diploid eggs resulting from the fertilization with only one kind of spermatozoa give females, whilst haploid eggs develop into males. For the Aphidæ the complete relationship between the chromosomes and the cycle is known. It appears, therefore, to us that every attempt to regard the relation of the sexual cycle to the sex problem from any other standpoint than that of the investigation of the factors regulating the maturation mechanism, or parthenogenesis, and spermatogenesis, is built on an insecure foundation.

The consideration of the matter naturally commenced with the observation of the conditions present in nature. Weismann was the first who recognized the great importance of the subject, and through exact biological studies of the generation cycles in the Daphnids, as well as through attempts to influence them experimentally, laid the foundations of our knowledge regarding it. He discovered first that the reproductive cycles of the individual species were rather different in type. In many species the formation of resting eggs was found to occur typically once only in the year—they were monocyclic; others exhibited a few to many successive periods of sexual and parthenogenetic reproduction—they were polycyclic. Others again, the acyclic species, appeared to have altogether lost the power of producing bisexual forms and reproduced continuously in a parthenogenetic manner. The production of the winter eggs, requiring fertilization, and the males are identical processes, the occurrence of the condition of bisexuality; for the first are not merely summer eggs which become winter eggs by fertilization, but are formed in a special manner, require fertilization, and without it perish. Only those processes which are connected with the formation of the final structures of the winter eggs with all their protective arrangements are dependent on fertilization.

Now Weismann found as a rule, and further faunistic studies also support it, that the monocyclic species occur in large lakes with a low degree of variation in environmental conditions—the most important being the freezing up in winter. The polycyclic species live, however, in the smaller ponds which are just as likely to dry up in the summer as to freeze in the winter, and resting eggs which survive through the bad periods are almost always at the disposal of these forms. Corresponding to the general direction of his ideas Weismann drew the conclusion that the generative cycle had been fixed hereditarily by natural selection. The whole phenomenon is thereby only intelligible from the point of view of phylogeny and must at the present time be independent of the factors of the environment which, earlier in the phylogeny of the species, have occasioned the selection. Certain experiments which he carried out no more permitted him to see any kind of hereditary influence of environmental conditions than his observations of the conditions in nature.

Exactly the same rhythmical phenomena were found in nature by Lauterborn[1] for the Rotatoria, whose conditions thus necessitated the same explanation as the above.

When these biological facts are brought into line with our previous deliberations, they indicate in our opinion that the different types of Cladocera possess heredity factors of different degree whose action is to call forth a definite rhythm in the ovarial conditions. This rhythm results in the chromosome mechanism of an egg being so influenced that the latter develops parthenogenetically into a female, parthenogenetically into a male, or becomes a resting egg requiring fertilization. In other words, the factor regulating the mechanism of maturation is an heredity factor whose action presents a rhythmical course.

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[1] Lauterborn, L., "Über die zyklische Fortpflanzung Limnetischer Rotatorien." Biol. Centralbl., 18, 1898.

Experimental investigation has now emphasized the question as to whether these rhythms are unalterable inherited phenomena or are called forth only by particular external conditions. After many wearying bypaths the following result has been attained with Rotatoria and Daphnids. We have to thank, above all, the workers of R. Hertwig's school, as well as Woltereck and his pupils, for the Daphnids, and Shull and Whitney for Rotatoria.[1]

If the appearance of males and winter eggs is designated as bisexuality, there are present within a line of Daphnids (Woltereck) or Rotatoria (Shull) regularly alternating periods of slight tendency to bisexuality and high tendency to such respectively. The following table shows such periods for the Rotifer *Hydatina senta* (after Shull), whereby the number of the male producers, which in the Rotatoria are identical with the producers of winter eggs, gives the measure for the height of bisexuality :—

Date	No. of ♂ Producing ♀	No. of ♀ Producing ♀	Date.	No. of ♂ Producing ♀	No. of ♀ Producing ♀
Jan. 16	2	24	March 14	0	44
19	0	24	17	0	38
22	1	35	20	0	42
25	3	33	23	0	23
28	19	46	26	8	40
30	14	46	29	36	48
Feb. 2	0	56	April 1	7	71
5	0	40	4	1	51
9	2	38	7	0	37
12	0	43	10	0	40
15	0	47	13	1	36
18	0	48	16	0	35
21	0	13	19	0	43
24	0	35	22	3	85
27	17	21	26	68	51
March 2	12	27	29	32	23
5	6	29	May 2	18	34
8	2	36	5	3	50
11	0	42	8	0	24

In the Daphnids these rhythms have been exactly studied, and Scharfenberg, Papanikolau, and Woltereck have determined in agreement that amongst the progeny of one female which has developed from a winter egg, the tendency to bisexuality grows with the number of generations and also with the number of individuals in a generation. The following table of Papanikolau's illustrates this in a striking manner (Fig. 104). The vertical columns give the number of young of a female, the horizontal give the parthenogenetic generations which occur. ○ indicates parthenogenetic females, ⊙ males, ◑ female with eggs requiring fertilization, ⦶ such which were not tested, ● those which died. No importance is attached to the latter since, according to Woltereck, the occurrence of degeneration after bisexuality

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[1] Scharfenberg, U., "Studien und Experimente über die Eibildung usw." Intern. Rev. Hydrobiol. Suppl. 2, III., 1910.—Papanikolau, G., "Experimentelle Untersuchungen über die Fortpflanzungsverhältnisse der Daphniden." Biol. Centralbl., 30, 1910.—Woltereck, R., "Über Veränderung der Sexualität bei Daphniden." Intern. Rev. Hydrobiol., 4, 1911.

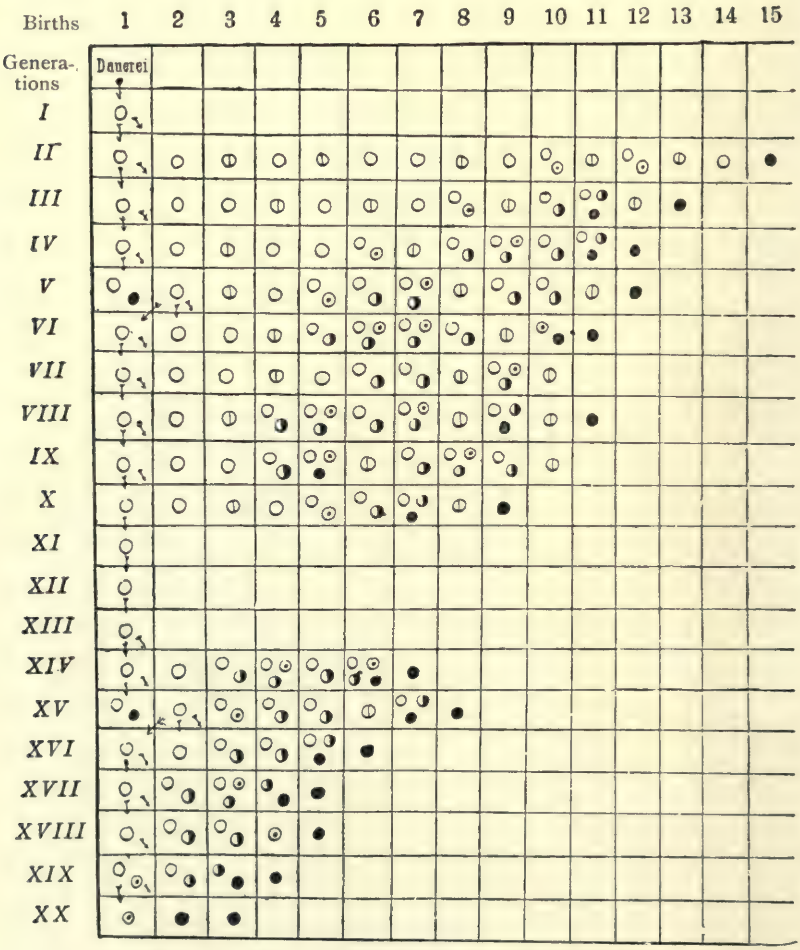

FIG. 104.—Diagram of the sexual cycle of a Daphnid.
After Papanikolau.

can be avoided by suitable culture conditions. There is no doubt that underlying this there is an inherited rhythm of bisexuality.

So far then one point is explained, namely, that the occurrence of bisexuality is determined by a definite inherited constitution, and rests as other hereditary characters on an hereditary factor, as Woltereck in particular has always claimed. The next problem is to determine how the hereditary constitution works physiologically in order to call forth the bisexuality, or on our conception to direct the maturation mechanism. The answer is to be deduced from attempts made to influence the hereditary effects by outer agents. It has been discovered that this is possible to a far-reaching degree, which is different, however, for different hereditary strains. Three groups of factors can be isolated which exert such an influence, namely, temperature, food, and the chemical nature of the environment, whereby Woltereck's assumption that all these act through the alteration of the intensity of assimilation is very probable. In general one can say that high temperature, rich food, and pureness of water favours parthenogenesis and represses bisexuality, whereas low temperature, hunger, and presence of waste products of metabolism in the water raises the tendency to bisexuality (Woltereck, Papanikolau, Langhans, Agar, Smith[1] for Daphnids; Maupas, Nussbaum, Shull and Whitney for Rotatoria; we refrain from entering into a discussion regarding the relative importance of the different agents). In the most extreme cases it has been possible to repress the bisexuality altogether and to obtain parthenogenetic lines, or conversely to enforce bisexuality even in the first generation. The possibility of this ability to influence the animals stands, however, in the closest connection with the inherited rhythm; periods of strong tendency to parthenogenesis, in which bisexuality cannot or can hardly be induced, alternate with labile periods in which the external factors are easily effective, and similarly there are periods of bisexuality where parthenogenesis cannot be induced at all or only with difficulty. But the quantitative value of this alternating susceptibility to external influences is hereditarily different for different races (Woltereck).

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[1] Langhans, V. H., "Über experimentelle Untersuchungen, usw." Verh. deutsch. Zool. Ges., 1909.—Agar, W. E., "Parthenogenetic and Sexual Reproduction." Journ. Genet., 3, 1914.—Smith, G., "The Life-Cycle of Cladocera." Proc. R. Soc. London, B. 88, 1914.—Shull, A. F., "Studies in the Life-Cycle of *Hydatina senta*." J. Exp. Zool., 8, 1910; 18, 1915.—Whitney, D. D., "The Influence of Food in Controlling Sex in *Hydatina senta*." *Ibid.*, 17, 1914.

So far as the nature of this inherited rhythm is concerned, the investigations of Woltereck and Shull show us distinctly that it is a question of a reaction which runs in a definite time (other conditions being equal). The table (of Shull) reproduced above shows a monthly rhythm for *Hydatina*. And Woltereck could show directly that, in spite of the experimental shifting of the course of the generations, the period of bisexuality occurred at its definite and proper time. Ephippia of *Hyalodaphnia*, which had lain dry four months longer than normal, gave females which immediately went on to bisexual reproduction. Woltereck draws attention particularly to the time factor. These and other analogous observations are naturally very significant, for they make the problem of sexual periodicity part of the problem of the great group of organic rhythms—the oestrus cycle, the rhythm of sleep movements, the periodic leaf fall, the change of hair, the moulting seasons and so on. It appears to us of very great importance that this should be clearly understood. We believe that the majority of the workers who have investigated cyclical sexuality have made (or make) the principal error of believing that they study thereby the physiology of sex determination. This is, however, as little the case as the study of the periodic moulting in birds (which concerns also the sex plumage and thus sex characters) gives us any insight into the sex determination problem. As a matter of fact this should be seen, for it is obvious in the Rotatoria, and almost as clear in the Daphnids, that the rhythm does not determine one or the other sex, but either females or both sexes. The rhythm is thus nothing but a period which rules the maturation mechanism of the egg (as well as the possibility of parthenogenesis) which then itself automatically determines the sex.

What the bee does "voluntarily" when it lays fertilized or parthenogenetic eggs according to needs, the Rotifers and Daphnids do under the compelling influence of an inherited rhythm, whereby in contrast to the bees but identically with other Hymenoptera a second parthenogenetic type arises, namely, one without reduction. This rhythm does not of course run within one individual life, but within a higher individuality constituted of a series of generations. The rhythmical sexuality rests, therefore, on an hereditary basis, and it calls forth in an undulating order a condition in the organism (or in a generation cycle of organisms) leading to the production of egg cells which can develop with or without parthenogenesis. It is exactly analogous to the hereditary basis which determines twelve hour sleep movements in a Mimosa. The working of this hereditary *anlage* can in both cases be more or less modified by outer conditions.

If this idea is correct, cyclical sexuality is no sex problem at all but a problem of heredity, and in particular a problem of the inheritance of characters with a periodic reactions norm. Woltereck is the only one who has so handled it consistently in these investigations, and has unfortunately fallen into the error of confusing it with the problem of sex determination in his final statements.

The view put forward here permits of the further details of this problem (in spite of its extraordinary importance for the question of the physiology of periodicity) being regarded as unessential for the physiology of sex. It may quite well attain extraordinary importance for the practice of sex control. The only visible way in which one can interfere in a directive manner with sex distribution—and that is popularly the control of sex—is to carry out experimentally what happens in the Daphnid or Aphid, with the different types of maturation division in the egg, or in the Aphid and the Rotifer where there is suppression of one kind of sperm. The essential condition to this is, however, the knowledge of the physiological state through whose agency the hereditable rhythm acts.

This direct cause may for all that we know now be chemical in nature. The investigations up to date have, however, only brought suggestions. In one case they have shown that the decision occurs in the maternal ovary—Woltereck's preinduction in Daphnids, the male and female producers in Rotifers, Aphids, and gall wasps—and so have led to the demonstration of G. Smith that the parthenogenetic Daphnids store up glycogen, the bisexual individuals on the other hand use fat as a reserve material. Out of these beginnings important knowledge may develop. This brings us naturally to the point where the matter touches the problem handled in the previous section.

CHAPTER VII

THE NUMERICAL RATIO OF THE SEXES

THERE is scarcely any branch of Biology in which so much nonsense has been talkėd as in the discussion on the connection of the numerical relations of the sexes to the problem of sex determination. The older investigators, who did not know of the mechanism of sex distribution, can be excused when they confused a shifting of the sex ratio with a sex determination. To-day, however, there is no room for excuse, as has been pointed out already by different authors. Where a shifting of the ratios of the sexes is experimentally successful, it can be due to many causes arising out of the mechanism of sex distribution; but only in the rarest cases is there a real sex determination, that is, either a directional influence on the distribution mechanism or an influencing of the physiology of sex differentiation. The cases of this kind have almost all been met with in the foregoing observations; they really belong in fact to quite another chapter. This brief reference is made in order to cut further reference out from the review of the problem of sex ratios.

An alteration of the ratios of the sexes through a directional influence on the distribution mechanism or on the physiology of sex differentiation occurs in the following cases :—

1. In experiments with zygotic intersexuality, such as those with the Gipsy moth, where 100 per cent males or females can be produced (by back crosses and F_2 in ratios of 3 ♀ : 1 ♂, 3 ♂ : 1 ♀, 2 ♂ : 1 ♀).

2. In experiments of the *Bonellia* type, where any ratio can be produced according as the larvæ get the opportunity of fixing themselves or not.

3. In all experiments with parthenogenetic forms, where the ratio can be influenced through enforcing one or the other type of reproduction, namely, with and without reduction, etc.

4. In experiments involving over-ripe eggs, or the chemical

or thermic treatment of unfertilized eggs, where the direction of the maturation division (in cases of female heterozygotism) or the susceptibility for one kind of spermatozoon (in male heterozygotism) may be influenced.

5. Where a hereditable mutation is present which in cases of female heterozygotism swings the maturation division always in one direction, as perhaps in Doncaster's female *Abraxas* line, or similarly in male heterozygotism when it suppresses one kind of sperm (Aphids, perhaps in mammals).

In all such cases naturally the definite numerical ratio of the sexes is related to the sex-determining processes.

In the great majority of cases variations from the normal sex ratio are due to other factors which have nothing to do with sex-determining causes. One must add, however, that particularly in the animal world there is little experimental material in this connection with which to begin. It has been shown statistically times without number that the ratio of the sexes present in nature corresponds only rarely to the expected 1 : 1. Some of the figures from the well-known compilations of Cuénot,[1] Schleip, Hertwig, and Lenhossek are given in the following table :—

	♂ ♀	ORDER.
Swine . . .	111·8 : 100	Mammalia
Oxen . . .	107·3 : 100	„
Rat	105·0 : 100	„
Rabbit . . .	104·6 : 100	„
Sheep . . .	97·7 : 100	„
Horse . . .	99·7 : 100	„
Pigeon . . .	115·0 : 100	Aves
Hen Fowl . .	94·7 : 100	„
Cottus . . .	188·0 : 100	Teleostei
Lophius . . .	385·0 : 100	„
Loligo . . .	16·6 : 100	Cephalopoda
Octopus . . .	33·3 : 100	„
Latrodectes . .	819·0 : 100	Arachnoidea
Lucilia . . .	95·13 : 100	Diptera
Macrodactylus . .	131·0 : 100	Coleoptera

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[1] Cuénot, L., "Sur la détermination du sexe chez les animaux." Bull. Sc. France-Belg., 32, 1899.—Lenhossek, M. von, "Das Problem der geschlechtsbestimmenden Ursachen." Jena, 1913.—Schleip, W., "Geschlechtsbestimmende Ursachen in Tierreich." Ergebn. Fortschr. Zool., 3, 1913.—Hertwig, R., "Über

Now it has often been pointed out that these variations from the normal can have very different causes. In the first place there are likely to be some errors in the statistics resulting from various possibilities in the computation of the sexes; then also there is the possibility of a different death-rate of the sexes during the period between the fertilization of the eggs and the fully-grown individual, and finally there is the unknown quantity, the primary ratio of the fertilized eggs.

A. Differential Elimination of a Sex

The first point, the error of the statistics, requires no discussion. It is evident that no conclusions can be drawn from the ratios found unless the fate of all the fertilized eggs is known. Then it may quite likely turn out that in most cases variations from the norm are due to a differential elimination of one sex after fertilization. It is striking how little exact material in regard to this point is available, although there are numerous occasional notes. The situation may be illustrated from a case out of our own experience.

In the old literature one often finds the statement that through different kinds of food the sex ratios of butterfly caterpillars can be modified. All these statements came to naught when it was known that even in the youngest caterpillars the sex is definitely determined (in normal cases). It was then pointed out (Standfuss) that eventual irregularities in the sex number could be explained by the different sensitivity of the rapidly developing males and more slowly growing females. The author was able to show exactly how this elimination worked. The caterpillars of the Gipsy moth make as a rule five moults; in certain races, however, pupation of the male caterpillars takes place after the fourth moult, female after the fifth.[1] The latter have then about ten days longer period of development. Now there are two malignant caterpillar diseases, Polyhedral disease and Flacherie. The first kills the animals at almost all stages. Its course varies considerably, but the greatest death-rate lies usually in the young

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den derzeitigen stand des sexualitätsproblems." Biol. Centralbl., 32, 1912.—Hesse-Doflein, "Tierbau und Tierleben." Bd. I., Leipzig, B. G. Teubner.

[1] Other combinations also occur with other races. See R. Goldschmidt, "Die quantitativen Grundlagen von Vererbung und Artbildung." Aufs. vortr. Entwicklungsmech., 1920.

and middle stages. Flacherie, on the other hand, breaks out more especially in old animals, and often reaches its high point only after the fifth moult. There is therefore no reason why Polyhedral disease should affect one sex more than another. It is otherwise with Flacherie. In the cases in which it only reaches its maximum after the fifth moult it must affect the females more than the males. Many of the latter are already pupæ, others still remain but only a short time longer in the caterpillar stage, so that the maximum of the infection does not touch them. It is therefore to be expected that with a rising death-rate in the later caterpillar stages the percentage of the females will decrease. In a large mixed epidemic of these two diseases in our broods we took accurate note of the death-rate, and it was possible to show that the selective elimination of the females followed exactly along the lines stated above. The normal ratio had been shown earlier to be 87·7 males to 100 females.[1] The infected broods gave when—

I. The death-rate after the fourth moult was more than 90 per cent—only males.
II. The death-rate after the fourth moult was more than 50 per cent—246 ♂ : 100 ♀.
III. The death-rate after the fourth moult was more than 20 per cent—177·8 ♂ : 100 ♀.
IV. The death-rate after the fourth moult was more than 10 per cent—142·7 ♂ : 100 ♀.
V. The death-rate after the fourth moult was less than 10 per cent—103·1 ♂ : 100 ♀.

When, on the other hand, the death-rate in the later stages was nil but an extraordinary high rate was present in the earlier stages, the sex ratio was almost uninfluenced, thus VI, death-rate 82·3 per cent, but none after the fifth moult = 105·6 ♂ : 100 ♀. This is without doubt a clear demonstration of how the selective elimination of a sex works; at the same time it warns one not to draw hasty conclusions from sex ratios.

In this case the manner in which the selective elimination of the females takes place is quite clear. In most other cases it is only possible to demonstrate the fact or infer it. Thus it is a frequent occurrence that in the hybridization of relatively widely separated forms only males are produced or strikingly many males. In many cases this may be due to inter-sexual transformation as in a series of Lepidopteron crosses [*Lymantra* (Goldschmidt), *Biston* (Harrison)] and perhaps certain pigeon crosses (Whitman-Riddle). But in other cases it may also be bound up with the general constitutional weakness of the hybrids, one sex of which is more affected than the other, just as one sometimes finds that one sex is more sensitive than another in the young stages. In this category perhaps come Guyer's[1] pheasant and guinea-fowl—common fowl hybrids. But the accuracy of his statements, namely, that there is a marked excess of males in such hybrids, is strongly contradicted by Poll who found quite a normal distribution of the sexes.

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[1] Goldschmidt, R., und Poppelbaum, H., "Erblichkeitsstudien an Schmetterlingen, II." Ztschr. indukt. Abst., 11, 1914.—Goldschmidt, R. "Untersuchungen über Intersexualität." Ztschr. indukt. Abst., 23, 1920.

There is still another possibility for the selective elimination of a sex, namely, the possibility of the presence of hereditable "Lethal factors" which are sex linked or not in their inheritance. A lethal factor is an hereditary factor, the presence of which in an individual (often only in the homozygotic condition, often also in the heterozygotic condition) renders it incapable of existence. Although the special kind of pathological condition which this factor calls into being is not always known, there can be no doubt of the fact itself which is well known to all workers in Genetics. If such a lethal factor is inherited in the sex-linked condition the following situation will arise, a case made clear by Morgan in connection with *Drosophila*.

Morgan found a race which always produced twice as many females as males. He hybridized a normal-eyed female of this race with a white-eyed male. It will be remembered that white-eye condition is a sex-linked factor. F_1 should be red eyed. The F_1 female crossed with white-eyed males should give red and white-eyed members of both sexes in equal proportions. It gives, however, no red-eyed males. Now since the males are heterozygotic, the X chromosome of the red-eyed male comes, as Fig. 105 shows, from its grandmother with which the experiment began. If this contained, in addition to the red factor, a lethal factor, the bearer must die. The female contains, however, a second X chromosome and is therefore not affected—it is only when both X chromosomes contain these lethal factors that it also is incapable of existence.

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[1] Guyer, N. C., "On the Sex of Hybrid Birds." Biol. Bull., 16, 1909.

B. Primary Deviations from the Normal Zygotic Number

The other possibility of the production of abnormal ratios appears more interesting. According to the laws of probability equal chances of fertilization by the two kinds of germ cells of the heterogametic sex is to be expected. Now there is a possibility that one of the two combinations may occur more frequently than the other.

As a matter of fact a series of possible causes for this are to hand, two of which are at least supported by facts. The first circumstance to be taken into account is that the two kinds of gametes may not be produced in like numbers, and chance fertilization will therefore not lead to equal numbers of the sexes being produced. The second possibility is that the different gametes may be produced in equal numbers, but that the two sorts produced by the

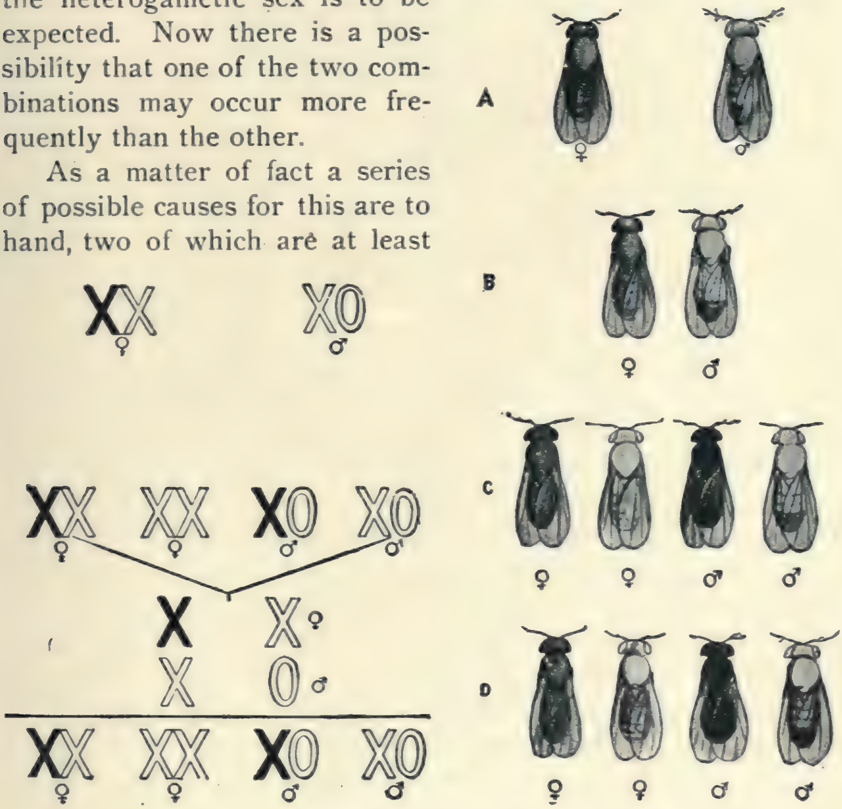

Fig. 105.—Diagram of the inheritance of a sex-linked lethal factor in *Drosophila*.

(The black X chromosome carries the lethal factor as well as the factor for red eyes. On the left, the chromosome conditions are shown.)

A, red eyed ♀ carrying the lethal factor in one X, is bred to a normal white-eyed male; B, the red-eyed daughter is bred again to a normal white-eyed male, giving theoretically the four classes shown in C, but one of the classes fails to appear, viz. the red-eyed male (shaded almost black in the illustration). The analysis shows that this male has the lethal X. A sister has also this factor in the X chromosome, but is saved by the other X. She is the red-eyed female. If she is bred to a white-eyed male, she gives the result shown in D, four classes, of which one, the red-eyed male, fails to appear.

After Morgan.

heterogametic sex have different chances of fertilizing or being fertilized.

1. The Primary Numerical Ratio of the Gametes

The obvious presupposition of the chromosome mechanism of sex distribution, as of the whole Mendelian factor theory, is that the different kinds of gametes are formed according to the laws of chance in equal numbers. That this is usually the rule is demonstrated by the fact that in hybridization experiments with large numbers, the numerical conditions of the resulting classes agree with the probabilities within the limits of probable error. In many cases this agreement is most complete. There are cases, however, where certain classes are typically too large and others too small.

If one excludes the cases which are explained by factorial exchange (crossing over) there can be no doubt that the gametes, other sources of error being cut out, are not produced in exactly equal numbers. Detlefsen has tried to demonstrate this directly in the case of rodents. We do not know of course on what such a feature depends. It is possible that in cases with female heterozygotism, physiological conditions in the protoplasm influence the direction of the maturation divisions (see parthenogenesis and over-ripeness). It is possible that with male heterozygotism one kind of sperm cell is more frequently affected than the other by the cell degeneration so frequently met with in the testis (see spermatogenesis of Aphids).

Of exact zoological investigations we have only the work of Seiler already referred to (see p. 211) which demonstrates directly by observation and experiment that with female heterozygotism sex ratios varying from the norm can be explained by the direction of the maturation divisions.

2. Different Chances of the Respective Gametes

The shifting of the sex ratio, through the possibility that the two kinds of gametes, although present in equal numbers, might not have the same chances of achieving fertilization, could take place in different ways. With female heterozygotism the one kind of egg for some unexplained reason might be more susceptible to normal fertilization than the other. If Riddle's observations in regard to the physiological difference of the male and female pigeon eggs are right, they would provide the actual foundation for a differential condition of this kind. For it is well known from studies on the physiology of fertilization (Loeb, Lillie, and others) that the normal fertilization demands a number of special preliminary physiological conditions.

No experiment, however, which actually demonstrates the presence of such a phenomenon is known to us. With male heterozygotism a differential condition could be just as much due to the state of the egg favouring the penetration by one kind of sperm more than the other, as to different conditions of the two sorts of spermatozoa.

So far as the first possibility is concerned, namely, the differential fertilization ability of the egg in regard to the two kinds of spermatozoa, there is a little evidence that can be considered as of a supporting nature. But it must be regarded merely as tentative, since it has not shown itself altogether free from objection. Statistical studies (which *a priori* are to be received somewhat sceptically when the data have not been collected under experimental control) have often shown that the ratio of the sexes undergoes periodic changes. Miss King has put together the following table from the published statements of Wilckens and Heap:—

Animal.	Total No.	No. of ♂ : 100 ♀		Whole Year.
		Warm Months.	Cold Months.	
Horse . . .	16,091	96·6	97·3	97·9
Cattle . . .	4,900	114·1	103·0	107·3
Sheep . . .	6,751	102·1	94·0	97·4
Pig . . .	2,357	115·0	109·3	111·8
Wolfhound . .	17,838	126·3	122·1	118·5

In her own investigations, which Miss King carried out under reliable experimental conditions, the same features were demonstrated for the white rat.

Fig. 106 expresses the results graphically. A is the curve for the ratio in the experiments of the years 1911-13, B for 1914, and C is the average of both. There is a distinct periodicity with a minimum for males in March and in September and a maximum in the height of summer. *A priori* this periodicity is as likely to be conditioned by the state of the eggs as by that of the sperms. (Male heterozygotism is the rule in mammals.)

The following facts, however, point to the greater probability of the eggs being responsible. It has often been stated on the ground of statistical investigations that the sex ratio in the progeny of a young mother is different from that amongst children of old mothers (Bidder, Punnett, Wilckens, Copeman, and Parsons).[1] Miss King found that this was supported by her own experiments, as the following table shows :—

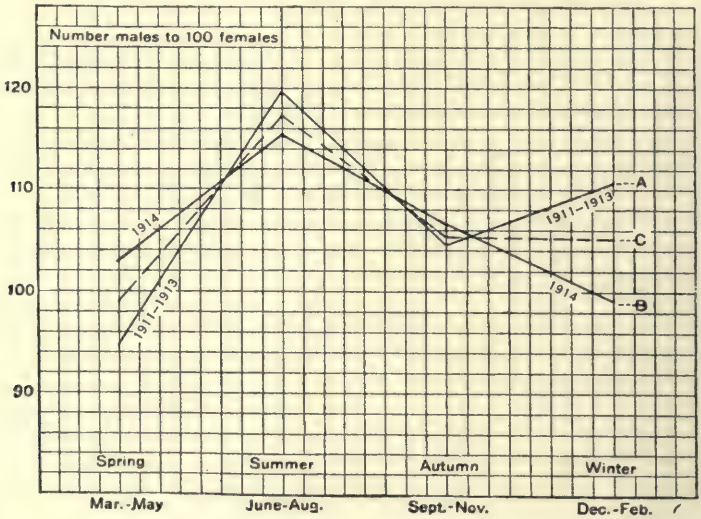

FIG. 106.—Curve showing the periodicity of the sexual conditions amongst rats during the years 1911-13 (A), 1914 (B), and the average (C). The curve gives the number of males to 100 females. After H. D. King.

Sequence of the Litters.	Number of Litters in Series.	Individuals.	♂	♀	♂ : 100 ♀.
1	21	131	72	59	122·0
2	21	162	85	77	110·4
3	18	127	64	63	101·6
4	15	96	41	55	103·1

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[1] Wilckens, M., "Untersuchung über das Geschlechtsverhaltnis und die Ursachen der Geschlechtsbildung bei Haustieren." Landwirtsch. Jahrb., 15, 1886.—Heape, W., "Notes on the Proportion of Sexes in Dogs." Proc. Cambridge Phil. Soc., 14, 1908.—Bidder, F., "Über den Einfluss des Alters der Mutter auf das Geschlecht des kindes." Geburtsh. Gegn., 11, 1878.—Punnett, C., "On Mutation and Sex Determination in Man." Proc. Cambridge Phil. Soc., 12, 1905.—Copeman, S. M., and Parsons, F. A., "Observations on Sex in Mice." Proc. R. Soc. London, 73, 1914.—King, H. D., and Stotzenburg, J. H., "On the Normal Sex-ratio," etc. Anat. Rec., 9, 1915.

The first litters of a female here contain more males than the later ones. The natural implication is that the physiological condition of the eggs is responsible. Should the deductions drawn from these results turn out to be correct, there would be no difficulty in bringing them into line with the other biological data. It is known in connection with the Daphnids and Rotifers that an inherited cycle brings about definite conditions in the egg which regulate a maturation and fertilization mechanism. It is also known that in the Mammalia there are other hereditable rhythms which are bound up with the reproductive organs —as, for example, ovulation, rutting, and cyclical changes in the testis. Furthermore, we know that in the Daphnids the number of broods, as well as the number of generations, plays a rôle in the cycle. The assumed cyclical condition of the eggs constitutes, therefore, the same problem as that of other rhythms, and thus from the point of view of the sex problem may be regarded as explained.

So far now as the second possibility is concerned, namely, a difference in the behaviour of the two kinds of spermatozoa in the competition for fertilization, there is already evidence from many sides indicating that it is possible to explain divergences from the normal in sex ratios on these lines. There is also diverse material which seems to support the correctness of the assumption even if there be no undoubted proof.[1] In the first place mention must be made of the great difference in the size of the two kinds of spermatozoa (discovered by Wilson and confirmed by Zeleny[2] through numerous measurements) in cases in which male heterogametism has been demonstrated. Fig. 107 shows a bimodal curve which Zeleny obtained from such measurements and the two parts of the curve are almost equal, which corresponds to the expectation. It is quite conceivable that the two sorts of sperms have different speeds and therefore different chances of fertilization.

Certain experiments indicate that it is possible to influence the two kinds of sperms in such a way that a different fertilization ability is actually visible. This is very clearly shown in the investigations of Stockard[1] and Papanikolau on the influence of parental alcoholism on the progeny. These authors showed that more damage occurred amongst the progeny of alcoholized fathers (guinea-pigs) than amongst the progeny of alcoholized mothers. The sperms suffered, therefore, the greater damage. But amongst the progeny of alcoholized fathers the daughters showed a greater tendency to die than the sons. The same held good for the progeny of alcoholized paternal grandfathers, which suffered even greater damage than the progeny of alcoholized fathers. These experiments indicate that some definite damage is done more to one kind of sperm (in this case the female producing) than to the other. And if this is so, one can draw the conclusion that it is possible, by means of definite physiological and pathological agents, to influence one kind of spermatozoan in its power of fertilization more than the other. This postulates of course that there is a kind of fight or competition for fertilization amongst the spermatozoa. That such is actually the case has been very beautifully demonstrated by Cole and Davis.[2] They mated the same rabbit at the same time with two males of different hereditable nature, so that one could determine which

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[1] Although we limit ourselves here to the animal kingdom, it must at least be noted that in the plant world the evidence of Correns and Renner can be adduced. Of course the pollen tube cannot be compared directly with the spermatozoan but with the whole male individual.

[2] Zeleny, C., and Faust, E. C., "Size Dimorphism in the Spermatozoa from Single Testes." Journ. Exp. Zool., 18, 1915.

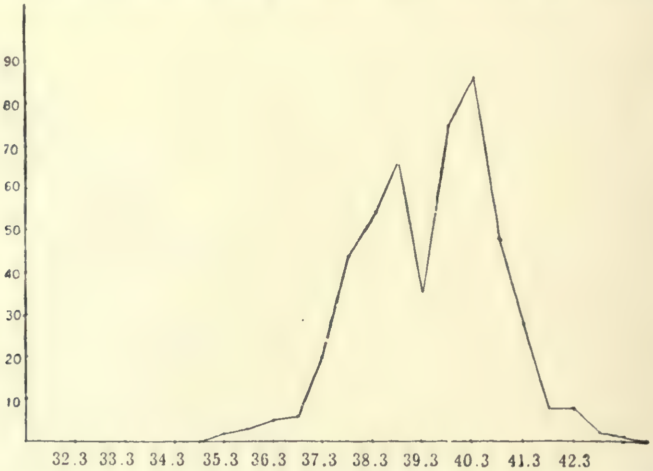

Fig. 107.—Frequency curve for the length of head amongst 493 spermatozoa of the Hemipteran *Lygæus Kalmii*. After Zeleny.

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[1] Stockard, Ch. R., and Papanikolau, G., "A Further Analysis of the Hereditary Transmission of Degeneracy," etc. Amer. Natur., 50, 1916.

[2] Cole, L. I., and Davis, C. L., "The Effect of Alcohol on the Male Germ-Cells Studied by Means of Double Matings." Science, N.S., 39, 1914.

was the father by the colour of the young. One male showed itself more potent than the other inasmuch as the majority of the young in the litter always came from it. When the sperms from this same male were damaged through alcoholization no young were produced by it in the corresponding experiment. They *were* still produced, however, if this male were used alone for fertilization. The alcoholized sperms were thus capable of fertilization, but were beaten in the competition by the normal spermatozoa.

This is perhaps the place to discuss the relations between the time of ovulation and the sex ratio. Thury pointed out long ago that cows which were fertilized at the beginning of the heat produced relatively many female progeny, whilst on the other hand late served cows gave an excess of male calves. His far-reaching deductions from these observations have been much discussed and disputed. Pearl and Parshley believed that they could confirm the discovery, but after a new statistical investigation they withdrew from this position.[1] References by Siegel to man are touched upon in the next section. Since the female sex is the homozygotic one, it is no use assuming that there is any directional influence on the maturation mechanism. The assumption of a selective reactivity of fresh and old eggs for two sorts of sperms cannot *a priori* be overthrown in the light of the different behaviour of eggs in hybridization experiments towards different sperms, and the possibility of influencing such eggs through the medium. (Examples: Attainment of crosses in one direction, failure of the reciprocal cross. Facilitation of heterogeneric crosses by raising the alkalinity of the medium.) Since in this connection it has been demonstrated that it is a matter of the physico-chemical conditions of the egg surface (Herbst, Loeb), it is very likely that during the sojourn of the egg in the oviducts these conditions gradually change and that the two kinds of sperms react differently to this alteration. Finally the distance of the egg from the tuba together with a different motility of the two kinds of sperms, might have something to do with the question. Owing to lack of information based on experiment, however, the solution is not yet possible.

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[1] Thury, T., "Über das Gesetz der Erzeugung der Geschlechter." Leipzig, 1863.—Pearl R., and Parshley, H. M., "Sex Determination in Cattle." Biol. Bull., 24, 1913.—Pearl, R., "Report of Progress on Animal Husbandry Investigations in 1916." Rep. Maine Agr. Exp. Stat., 1917.

In fact the whole chapter of the numerical ratio of the sexes is not altogether satisfactory in other respects.

C. Summary

In view of the importance which appertains to a clear conception regarding the sex ratio in its significance for the sex problem, it is desirable to restate the possibilities for whose assumption there is justification at present, especially as there is the likelihood of reading the possibility of a practice of sex control from such a compilation. The variations of the sex ratio from the norm 1 : 1 might be occasioned:—

1. Through influencing the physiology of sex differentiation in cases of transformation of sex. The changed sexes would represent the most extreme form of

    (*a*) Zygotic intersexuality.
    (*b*) Hormonic intersexuality.
    (*c*) Transitory intersexuality.
    (*d*) Intersexuality through activation.

2. Through a directional influence being exerted on the mechanism of sex distribution

    (*a*) By the aid of parthenogenesis.
    (*b*) In over-ripeness and temperature experiments.
    (*c*) By the presence of an inheritable constitution which only allows the maturation division in the egg to take place in one direction or causes one sort of sperm to perish.

3. Through special features associated with the otherwise normal mechanism of sex distribution such as—

    (*a*) Through the selective elimination of a sex.
        α. Where there is different developmental biology of the two sexes.
        β. Where there is a different resistance power of the developmental stages of the two sexes to constitutional or external damage.
        γ. In the presence of a sex linked lethal factor.
    (*b*) Through the production of zygote numbers which differ from the norm at the outset.

α. In consequence of primary numerical differences between the two sorts of gametes produced by the heterozygotic sex (belongs partly to section 2).

β. In consequence of the gametes having different chances of fertilization caused by—

αα. Different attractive power of the two sorts of eggs for the sperms.

ββ. Different susceptibility of the eggs to the two kinds of sperms.

γγ. Different activity of the two sorts of sperms.

δδ. Different sensitivity of the two sorts of gametes of the heterozygotic sex to the deleterious features of the physiological environment in the widest sense.

CHAPTER VIII

SEX DETERMINATION IN MAN

THERE is no real ground for treating sex determination in man separately from that of the rest of the animal kingdom. It is only justified for sentimental reasons, as well as on the ground that the conditions in man cannot be studied experimentally at all, or only with difficulty, and therefore their explanation must depend on comparison with the other mammals. In addition to this we have the interest—to a great extent unscientific—which the question has always aroused and which has led to the most absurd ideas and theories. These are still being produced and put forward every year, and consequently a special statement of the conditions in man, taken apart from the rest of the work, appears to be desirable. It will be presented in the same sequence as the other material.

A. Mechanism of Sex Distribution

1. The Chromosome Mechanism

The elucidation of the chromosome mechanism of sex distribution in man has turned out to be rather difficult, for the material, as in the case of some other animal groups—the birds, for example—does not appear to be favourable. The older reports, which did not take into account the possibility of sex chromosomes, indicated a diploid number of twenty-four chromosomes in man (Hansemann, Flemming, and Duesberg). Guyer,[1] who investigated the spermatogenesis with reference to the sex chromosomes, found only twenty-two chromosomes, and believed that at the maturation divisions two sorts of spermatids were formed, some with ten and some with twelve chromosomes. This was contradicted by Gutherz and also by all other observers. Montgomery again found twenty-four as the normal number of which two formed an XY pair. In the maturation divisions these were in many cases separated in the manner required by the digametism scheme and half the sperms contained 11 + X, the other half 11 + Y. But in many cases the distribution was different, so that finally no fewer than four to six kinds of spermatozoa were produced. From this view again Winiwarter completely diverged. He found forty-seven chromosomes to be the normal number in the spermatogonia, and in the maturation divisions two kinds of sperms were produced, those with twenty-three and those with twenty-four chromosomes. He also found forty-eight chromosomes in the ovary of a fœtus, so that we have typical male heterogametism with forty-seven chromosomes as the male number and forty-eight as characteristic of the female. An attempt has been made to clear away the extraordinary differences between the discoveries of Guyer and Montgomery on the one side, and Winiwarter on the other, on the ground that the first-named authors investigated negro material, the latter European. Cases are known in both the animal and plant worlds where closely related races differ in the chromosome numbers in the relations n : 2n (for example, *Ascaris*, *Artemia*).

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[1] Guyer, M. F., "Accessory Chromosomes in Man." Biol. Bull., 19, 1910, and Science, 39, 1914.—Gutherz, L., "Eine Hypothese zur Beurteilung des Problems, usw." Sitzungs-Ges. naturf. Freunde, Berlin, 1912.—Montgomery, Th., "Human Spermatogenesis, Spermatocytes, and Spermiogenesis." Journ. Ac. Nat. Sc. Philadelphia, 15, 1912.—von Winiwarter, H., "Etudes sur la spermato-génèse humaine." Arch. Biol., 27, 1912.—Duesberg, J., "Sur le nombre des Chromosomes chez l'homme." Anat. Anz., 28, 1908.

But at the same time it was forgotten that Hansemann, Flemming, and Duesberg had investigated Europeans and also found twenty-four chromosomes as the normal number. The investigation of Wieman[1] has been carried out on negro material and also on white, and he finds the normal number always twenty-four. Among these there is an XY pair that as usual is distinguished by its special conduct during the spermatogenesis. In the second spermatocyte division it is separated with one half of the autosomes, and the result is female-determining sperms with 11 + X and male-determining with 11 + Y chromosomes.

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[1] Wieman, H. L., "The Chromosomes of Human Spermatocytes." Amer. Journ. Anat., 21, 1917.

The latest reports of Grosser and Painter[1] are again diametrically opposed to this. The first author finds in part of his material twenty-four chromosomes, but in another part forty-eight is the normal number as his photogrammes show most clearly. Painter finds forty-seven or forty-eight chromosomes. Under these circumstances it appears rather probable that both numbers actually occur. Painter's view agrees, therefore, with that of many other authors in that two sorts of sperms are produced. Nevertheless the details cannot yet be regarded as completely cleared up.

2. Sex-linked Inheritance

We have already seen how the connection between the chromosome investigations and the Mendelian factorial theory was disclosed in regard to sex through the facts of sex-linked inheritance. In man also a whole series of sex-linked characters are known whose analysis agrees perfectly with the assumption of male heterogametism. The best-known cases are hæmophilia and colour-blindness. Others are night-blindness (hemeralopia), inherited muscular atrophy, a form of hypospadia, and even certain psychical fundaments such as the wanderlust (according to Davenport).[2] The genetic investigation of these conditions is naturally much more difficult in man, since it depends solely on statistical material in which the combination brother and sister, in particular, is altogether absent. Another difficulty is added by the fact that many diseases and abnormalities, which appear identical, are different in their inheritance. Thus there is a sex-linked hypospadia and one that is inherited as a direct dominant; a sex-linked colour-blindness and perhaps several other types. Of course this is not without analogies in the animal world. There are insects with dominantly inherited melanism and also sex-linked melanism. But in human genealogies it presents a greater difficulty. Nevertheless there are sufficient cases which are quite clear.

Hæmophilia is an example of these, the hereditary incoagulability of the blood from wounds.[3] The defect is only found in the male sex and omits a generation in its inheritance. If a male with the defect marries a healthy woman, all the children are healthy and even the offspring of the sons are without the defect. On the other hand, half the sons of the apparently healthy daughters turn out to be affected. This defect only manifesting itself in the males is therefore only handed on by apparently healthy (normal) females. In Fig. 108 the famous genealogy of the hæmophilic family Mampel is reproduced once more (the affected individuals are represented by black circles)—a glance will show the manner of inheritance.

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[1] Grosser, O., "Ueber die Chromosomenzahl beim Menschen." Anat. Anz., 54, 1921.—Painter, Th. S., "The Y Chromosomes in Mammals." Science, N.S., 53, 1921.

[2] Davenport, C. B., "The Feebly Inhibited." Carn. Inst. Publ., 236, 1915.

[3] Bauer, V., "Zur Vererbung und Konstitutions-pathologie der Hæmophilie." Dtsch. Ztschr. Chirurg., 176, 1922.

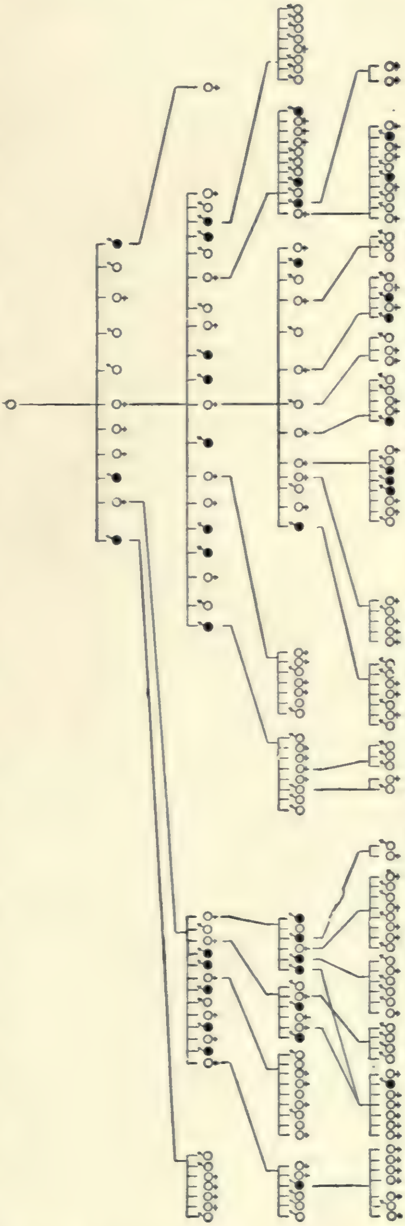

FIG. 108.—Genealogy of the hæmophilic family Mampel. After Lossen from Gruber-Rüdin.

We have discussed in detail on an earlier page how sex-linked inheritance is fully explained by the assumption that the factor for the character concerned is contained by the X chromosome. This holds good also for man, as is indicated by the diagram, Fig. 109 (from Wilson). Here it is taken for granted that the heterogametic male sex has only one X chromosome, the female two. If it is correct, however, that the male contains an X and a Y, one must insert a Y in the place of the dash which indicates "no X." The X chromosome carrying the defect factor may be termed the defective X chromosome; it is printed as 𝕏 in the diagram. The factor is recessive. Thus if a healthy woman married a defective man the sex chromosome conditions are such as is shown in the first line of the diagram. Since the X chromosome of the male has no partner, a male with a defective X chromosome must naturally be visibly defective. The next line shows the gametes produced by these parents, and the third the two possible combinations in the children of the F_1 generation. One sees at a glance that all the sons must be healthy and also unable to carry on the defect because they do not possess any defective X chromosome. The daughters are also healthy because healthiness dominates defectiveness. Notwithstanding this they possess a defective X chromosome through which they are carriers of the abnormality If such heterozygotic females marry healthy males, the four sorts of gametes depicted in the fourth line may combine to give the four combinations of the fifth line. A glance shows that all the daughters are sound, but that half of them again possess a defective X chromosome and can thus pass on the defect. Of the sons half are healthy, half are defective. It will be

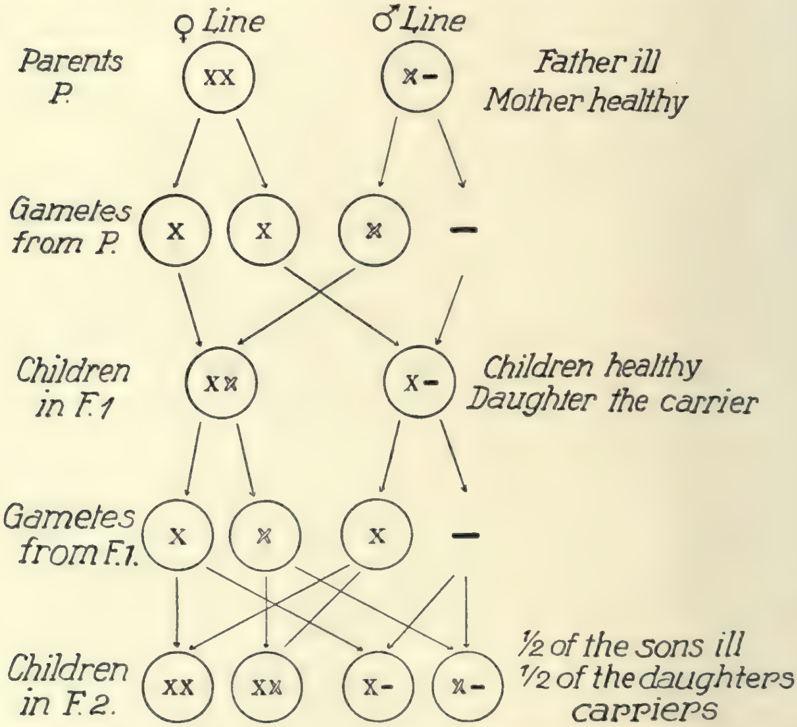
♀ Line
♂ Line
Parents P.
XX
X-
Father ill
Mother healthy
Gametes from P.
X
X
X
-
Children in F.1
XX
X-
Children healthy
Daughter the carrier
Gametes from F.1.
X
X
X
-
Children in F.2.
XX
XX
X-
X-
½ of the sons ill
½ of the daughters carriers

FIG. 109.—Diagram showing the relations of the sex chromosomes in the inheritance of colour-blindness and hæmophilia. After Wilson.

seen that this remarkable type of heredity can now be very simply explained. (Naturally this does not mean that all the possible combinations in so far as sex-linked heredity is concerned have been completely explained and cleared up.) We may affirm, therefore, that in man also the mechanism of the inheritance of sex is understood. It belongs to the same type as that in the fly *Drosophila* to which reference has so often be made.

3. Single-Egg (or Monozygotic) Twins

The occurrence of polyembryony is also known in man in the form of the so-called single-egg or monozygotic twins. Although, as one can naturally understand, nothing very exact is known of their origin, comparison with other mammals indicates that some kind of fission of the germ cell at an early embryonic stage is responsible. The identity of certain somatic characters in the twins (finger prints) can be brought forward as supporting this idea. Both the members of these single-egg twins are always of the same sex. Statistical studies of twin births show that about a quarter of all twins are single egged. According to Nichols the following combinations of twins is found :—

♂ ♂	♀ ♂	♀ ♀
234497	264098	219312

thus a relation of the three types in the proportions about 1 : 1 : 1. According to the laws of probability it should be 1 : 2 : 1 if all twins were the result of the simultaneous production and fertilization of two eggs; the excess of ♂ ♂ and ♀ ♀ pairs is thus probably due to the occurrence of single-egged twins.[1]

B. The Nature of Sex Inheritance

We obtained most of our knowledge of the nature or physiology of sex determination from the facts concerning the different types of intersexuality and related phenomena. The human conditions also offer a small contribution to our knowledge of this subject, and it agrees well with the results obtained by experiment on other animals.

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[1] See Summary of Material in Newman, H. H., "The Biology of Twins." Chicago, 1917.

1. Internal Secretions and Sex Characters

In considering hormonic intersexuality we started with the relation between the sex characters and the internal secretory glands of the gonads. This section of our subject has been very well investigated in man, for to a certain extent it is of practical importance, and there is some experimental material in the results of castrations which have been carried out for religious, medical, and other reasons.

The most detailed investigation of the problem is that carried out by Tandler and Grosz,[1] and we will follow their work although the conclusions drawn will not be identical with theirs. They investigated the Russian castrated sect, the Skopti, who are castrated for religious reasons in their youth. Their description runs as follows:—

"The skin colour of the face presents a characteristic yellowish tone, the skin is pale and poor in pigment. Wrinkles appear at a relatively early age, and correspond when fully developed not only with such as develop in the face of old people corresponding to the mimetic movements, but are strongly marked on other parts of the facial skin also. The skin of the trunk is pale, wax-like, and poor in pigment even in dark-haired persons. The hair of the head is usually thick and the eyebrows well developed.

"The face is usually beardless, on the cheeks and on the upper lip a slight development of hairs (lanugo) is noticeable. On the lateral parts of the upper lip and on the chin one often finds longer hairs.

"It is a striking fact that old Skopti possess a rather well-marked beard development on the chin and above the arches of the mouth, whilst the middle part of the upper lip, the lower chin region, the cheek and the upper neck region, which also in man develops a rich beard growth, remains hairless.

"The beard development which has been observed, corresponds most closely in its localization and nature to that which frequently appears on old women.

"The whole trunk and the perinæum are completely hairless as also the lower extremities, especially the lower parts of the legs.

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[1] Tandler, J., und Grosz, L., "Die Biologischen Grundlagen der sekundären Geschlechtscharaktere." Berlin, 1913.

"Sparsely developed arm-pit hairs are regularly demonstrable. The pubic region is sparsely haired, and the boundary of the hairy region against the lower part of the abdomen is quite characteristic. Whilst in normal men the upper boundary of this hair extends towards the navel in the middle line (that is, the upper line boundary has the form of an angle ∧), in the Skopti, just as in women, the boundary is horizontal."

In addition there are regional, and often very considerable, fat deposits. So far as the larynx is concerned, the authors believe that it is not female but has remained at an infantile stage; the voice is supposed to resemble that of a boy at the period when the voice is breaking.

So far as the genital apparatus is concerned the following has been determined:—

"The prostate and seminal vesicles persist in a more or less infantile condition. In this there is a marked expression of the functional independence of the *uropoietic* and reproductive apparatus. Whilst the Corpum cavernosum urethræ and the M. bulbo-cavernosus which surrounds the Bulbus urethralis present a state of development which corresponds to the age of the individual, the Corpora cavernosa penis and the M. ischio-cavernosus remain stable in their development, or perhaps even fall into the atrophy of inactivity. The penis remains far behind in its development and resembles that of a child in form and size."

Tandler and Grosz conclude from these facts that castration does not call forth the characters of the other sex, but only a standstill at a stage of immaturity, in other words, the production of an asexual form. We cannot altogether agree with this conclusion. The consequences of castration are very different in birds and mammals according to the species and the time of castration. In many cases castration calls forth intersexuality, in others the transplantation of the opposite kind of sex glands is necessary. It is clear that intersexuality as a consequence of castration is only possible for those organs which develop after the operation. Now of these there are only a few in mammals and in man. According to our general view these must be of the female type, and as a matter of fact this is the case. If we exclude the fat deposits, which may be related to the other metabolic conditions, the pubic hair covering differentiates after castration and it is female in type; the beard also develops in the female type.

According to Pelikan[1] the hair of the head also grows continually and does not fall out so much in advanced age. Furthermore, there are numerous notes on the development of mammary glands and broad nipples in cases of male castration, which are summarized in Kammerer's work,[2] and they cannot easily be explained away on the ground that gynecomastia does not occur in all eunuchs. We believe, therefore, that the effect of castration is a *moderate* intersexuality, whereby the sex modification only touches the parts which still have the two possibilities of differentiation.

Finally, it may be pointed out that it is claimed that the internal secretory action of the interstitial glands has also been demonstrated in man. In cases of cryptorchidism the spermatogenesis can be quite suppressed whilst these glands still exist. All the secondary sexual characters are then normal. A direct experiment has actually been made in this connection, for Lichtenstern[3] succeeded in transplanting a cryptorchic testis (thus one containing as he believes only interstitial tissue) into a soldier whose testis had been destroyed. The usual consequences of castration had already commenced to show themselves, but after the transplantation of the interstitial tissue a retrogression of all the castration effects was observed. It may be noted here that the same objection may be raised as on an early page, to the production of hormones by the interstitial tissue. The critics of the older view assume that some sperm elements are also present in the cryptorchid testis. This, however, is a more special problem.

Regarding early female castration, as also regarding the transplantation of opposite kinds of gonads, we have no reliable material.

The events which accompany late castration, or age degeneration of the gonads, are not very suitable for throwing much light on the sexual problem. Nevertheless it is possible, although one must proceed carefully, to compare some of the phenomena observed in women in such cases with the cock feathering of old birds. This applies in particular to the growth of hair (Friedenthal[1]).

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[1] Cited from Tandler-Grosz.

[2] Kammerer, P., "Ursprung der Geschlechtsunterschiede." Fortschr. naturwiss. Forsch., 5, 1912.

[3] Lichtenstern, "Behebung von Kastrations-folgen beim menschen durch Transplantation von cryptorchen Hoden." Münchn. Med. Wochenschr., 19, 1916.

2. Intersexuality

There can be no doubt that typical intersexuality also occurs in man. It is generally spoken of as pseudohermaphroditism. Its systematic consideration, however, is a matter of extraordinary difficulty. In the first place, nothing at all is known as to the cause, so that we cannot even say whether it is zygotic or hormonic. Then the types are so extraordinarily different that it is difficult to classify them correctly. Furthermore, we possess for the mammals, with the single exception of the freemartin, no systematic knowledge concerning the different possible higher intersexual stages. Consequently it cannot be stated with certainty what is the genetic sex of an intersexual. It is true that the anatomists distinguish a Pseudohermaphroditism femininus and a Pseudohermaphroditism masculinus. The insecurity of the ground for doing this will be clear from a comparison with the freemartin. Here the outer genitalia are chiefly female, the internal male, yet the animal is undoubtedly genetically a female. A human intersex with an analogous structure would certainly be considered a case of Pseudohermaphroditism masculinus. As the individual would probably be brought up as a girl on account of the external genitalia, but would have male instincts on account of the internal secretory activity of the testis there would result a beautiful case of error of sex and the authorities would declare the individual male with slight intersexuality. Nevertheless the individual would be genetically a female intersex with a high degree of intersexuality.

Amongst the freemartins, however, there are also said to be cases where the external genitalia are more male.[2] A similar case in man would be undoubtedly denoted as a male with slight intersexuality of the external genitals. Yet it would really be an extreme case of female intersexuality with almost complete sexual exchange. These examples will make clear that it is impossible to determine the genetic sex of intersexuals and their degree of male or female intersexuality in man until an analogous case is known for each type in mammals whose genetic constitution can be determined. We may just refer in passing to the medical and juristic significance of these facts.[1]

---

[1] Friedenthal, H., "Beiträge zur Naturgeschichte des Menschen." Jena, 1908.

[2] The same thing is found in the female rodents which have been masculinized by transplantation (Steinach, Lipschütz).

When the cases of human intersexuality are studied—Neugebauer[2] has collected details of 2000 in his monograph—it is seen that in regard to both inner and outer genitalia every possible intermediate stage between the two sexes is to be found.

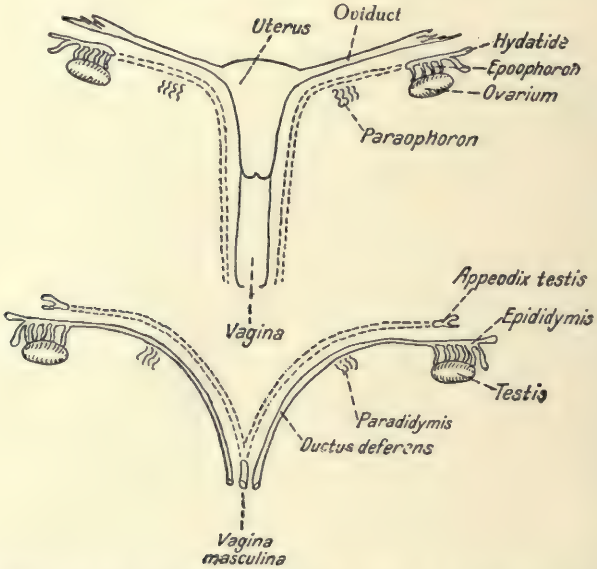


FIG. 110.—Diagram of the hermaphroditic genital *anlage* of a mammal. Mullerian ducts innermost, Wolffian ducts to the outside. After Broman from Plate.

The reader may be reminded first of the normal development of the human genitalia. The internal organs are laid down, as is well known, in the same manner in both sexes, following which they develop on different lines, as indicated in the diagram, Fig. 110. In this connection there remains normally traces of the fundaments of the other sex—thus in the male we have the uterus masculinus and remains of the oviducts, whilst in the female sex parts of the Wolffian ducts as the so-called hydatids and parovaria. The outer genitalia also commence with identical

---

[1] Goldschmidt, R., "Die Biologischen Grundlagen der konträren Sexualität und des Hermaphroditismus beim Menschen." Arch. Rassen-Gesellsch. Biol., 12, 1916.

[2] F. L. von Neugebauer, "Hermaphroditismus beim Menschen." Leipzig, 1908.

anlagen, and the male condition develops itself out of a condition resembling that of the female, as shown in Fig. 111. The chief features and the homologies may be taken for granted. The

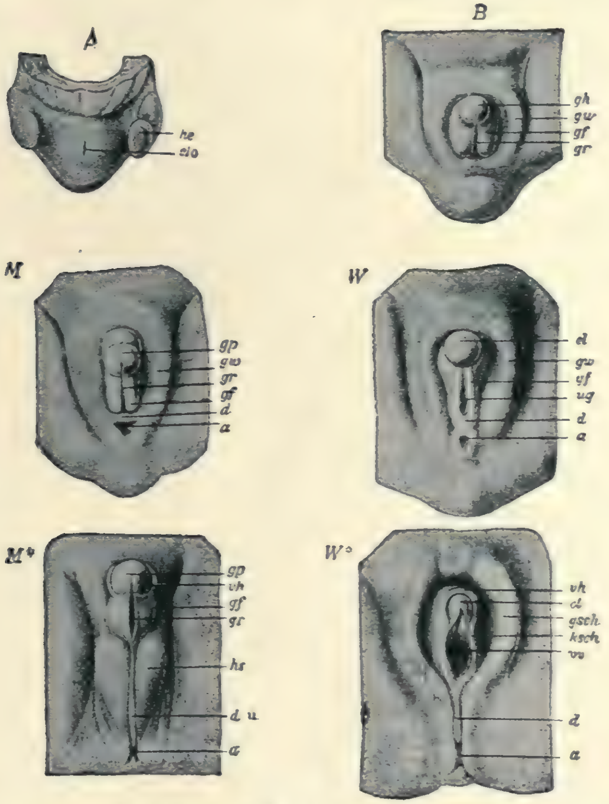


FIG. 111.—Models illustrating the development of the external genitalia.
From O. Hertwig.

A and B, young stages which are common to both sexes; M and M*, male development in 2½ and 3 months' old embryos. W and W* female embryos aged 2½ and 4½ months; he, hind limbs; clo, cloaca; gb, genital eminence; gf, lips of primitive urogenital opening; gr, primitive urogenital opening; gw, genital swelling; gp, glans; cl, clitoris; d, perinæum; a, anus, ug, entrance to sinus urogenitalis; W, vestibulum vaginæ; vh, foreskin; hs, scrotal sac; d and r, raphe perinei and scroti; gsch, labia majora; ksch, labia minora.

following chief types of intersexuality have been distinguished (after Neugebauer):—

1. External genitalia female and likewise the internal, but with developed Wolffian ducts in addition.
(Pseudohermaphrod. femin. int.)
2. External genitalia more or less hypertrophied (even erectile clitoris, which in some cases is penetrated lengthwise by the urethra). Labia more or less

fused. Urethral opening closed up. Internal genitalia female. (Ps. fem. externus.)

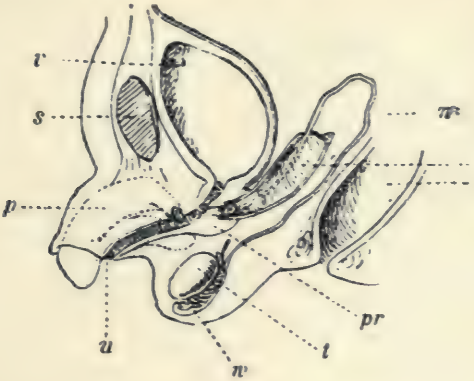
3. External genitalia male in character; ovaries, Mullerian ducts, and Wolffian ducts present. (Ps. fem. completus.)
4. External genitalia male in character; Testis and more or less rudimentary Wolffian ducts with derivatives present; more or less developed uterus, ducts and vagina. The testis often lies where the ovaries should be found. (Ps. masc. internus.)
5. External genitalia male with Hypospadia and more or less rudimentation of penis; all transitions to apparently female apparatus. Internal genitalia male. (Ps. masc. externus.) We may point out the resemblance of this category (the most frequent form of human intersexuality) to the structure of the freemartin. If the homology is correct, this would be female intersexuality!
6. External genitalia female. Testes, Wolffian and Mullerian ducts present. Canalis urinogenitalis persisting. (Ps. masc. completus).

In Fig. 112 (p. 247) diagrammatic figures of three types of intersexuality are depicted. They explain the foregoing without the need of further description.

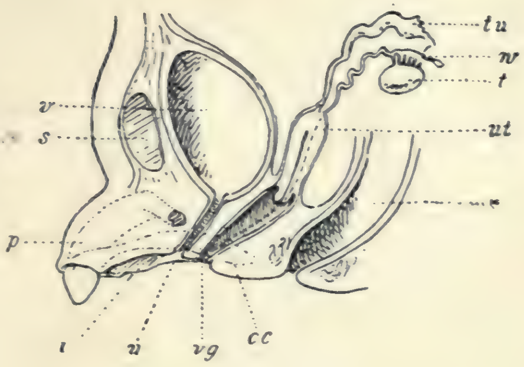
As pointed out above, a correct classification of these intersexual types is not possible at present. We know just as little of their causes. Lillie has, however, pointed out the very remarkable fact that the female hormones circulating in the maternal blood exert no influence on the male fœtus. There must be something present therefore which hinders this. A disturbance of this unknown mechanism might lead occasionally to male intersexuality through the influence of maternal hormones. This idea deserves to be kept in mind when considering at least some of the cases of male intersexuality. Another point worthy of note is that Neugebauer in quite a number of cases found intersexuality in several members of a family, thus perhaps some inheritable factor is concerned, analogous to the case in goats referred to above.

It is known with certainty that hypospadia is inherited as a dominant, and also at times as a sex-linked character. At the same time we do not know here whether we really have to do

I. Hypospadia of low grade with uterus masculinus.



II. Pseudohermaphroditism masculinus with total hypospadia, open mouth of vagina, labia minora; female arrangement of corpus cavernosum urethræ (vestibuli), fleshy uterus with oviduct; testis with epididymis, and vas deferens which runs downwards in the lateral wall of the vagina.



III. Pseudohermaphroditism femininus; externally the genitalia are completely male with slight hypospadia; labia majora completely fused; corpus cavernosum urethræ with female arrangement; vagina opens at colliculus seminalis into the pars prostatica urethræ. Ovary rudimentary.

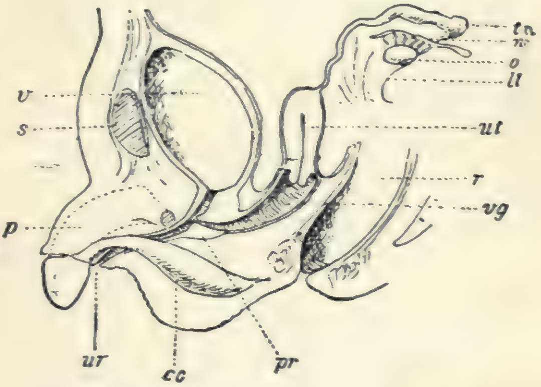


FIG. 112.—Three types of marked pseudohermaphroditism.
Semi-diagrammatic illustration of the sex organs in cases of pseudohermaphroditism.

v, bladder; s, symphysis; p, penis or penis like clitoris; u, aperture of urethra; r, rectum; cc, corpus cavernosum urethræ or vestibuli; vg, vagina; ut, uterus; pr, prostate; w, Wolffian duct of the Wolffian body (parovarium, epididymis, vas deferens, hydatids); l, labia min. (in II.); t, testis; tu, oviduct (closed in III.); ll, ligamentum latum.

After Marchand from Neugebauer.

with intersexuality or a repressing or inhibition of development such as occurs in hare lip. The latter appears to be the more probable, although Lipschütz (l.c.) tends to the first explanation. Steinach[1] again comes to another conclusion on the ground of his interesting experiments. In connection with his transplantation experiments (referred to earlier in this work) on rodents, this investigator attempted to implant into young castrated guinea-pigs testes and ovaries at the same time. The result was a kind of hermaphrodite development of the animals. If the gonads were implanted close to one another, they grew together as a kind of hermaphrodite gland which contained the interstitial tissue of both sexes. The somatic characters of the male were well developed, but of the female characters those which were normally rudimentary in the male were quite female in their degree of development—the teats and mammary glands. Psychically, male and female erotization alternated in these hermaphrodites. Steinach concludes from this, in reference to the so-called pseudohermaphroditism, that in all the many cases, where homologous and heterologous characters are found united in an individual with apparently one sexed glands, the position is "that these gonads are only one sexed in regard to the generative parts, but in regard to the internal secretory part they are bisexual; they contain, therefore, an hermaphrodite interstitial gland."

On the whole Sand has obtained the same result. It must be noted, however, with regard to all the remarks of these authors that we are still in a state of uncertainty as to the localization of the internal secretion. This has already been referred to and the question is still undecided. In fact at the present moment it almost appears as if the balance of evidence is against the localization in the interstitial cells. In other respects, however, the results of all these investigations (see also Athias, Moore, and Pézard) are full of contradictions in the details, and the conclusions are nothing like so clear as those relating to the lower animals. Before any safe practical application to man is possible one must have very much more experimental material. Theoretically all that has been brought forward in connection with the mammalia applies naturally to man.

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[1] Steinach, E., "Pubertätsdrüsen und Zwitterbildung." Arch. Entwicklungsmech., 42, 1916. For details see the latest comprehensive discussion by Harms: "Keimdrüsen und Alterzustand." Fortschr. der naturwiss. Forsch., XL., 1922.

In the meantime we regard it as probable that the pseudohermaphroditism is zygotic intersexuality. Since amongst the Mammalia the internal secretion of the sex gland is interpolated as the intermediary between the sex factors and the definitive differentiation, the consequence of zygotic intersexuality is intersexual hormonic activity. In two other important particulars we came simultaneously[1] from two quite different starting points to almost identical conclusions. One of these is the judging of homosexuality as a stage of intersexuality, the other is the abandonment of the distinguishing of hermaphroditism and pseudohermaphroditism since the former *may* be the highest grade of intersexuality (not *must* be—see above on teratological hermaphroditism). We concluded then, starting once again from our intersexuality studies, that one should be able to correct homosexuality by the transplantation of normal gonads. Steinach and Lichtenstern[2] have now actually carried out this experiment with success!

C. The Inheritance of Secondary Sex Characters

In regard to the condition of the secondary sex characters when human races are crossed which differ in these, little seems to be known. There is only the communication of Fischer[3] known to us, that amongst the South-West African "Bastards" (progeny of Hottentot-Boer crosses) there are all transitions in the female sex from almost Hottentot buttocks to the normal, as well as diverse forms of breasts. This suggests a Mendelian condition, as might be expected.

D. Hermaphroditism

Under the head of hermaphroditism we understand here as elsewhere the presence of sex glands of both kinds. Hermaphroditism could be the last member of the series discussed above under the title of pseudohermaphroditism and then it would belong to the last section but one. It could also belong to one of the groups of teratological hermaphroditism not yet analysed, or be gynandromorphism if such is indeed possible in the Mammalia. Actually we know of only occasional abnormalities, for which a safe explanation is not easily to be found. Amongst the most certain cases are the following: Gudernatsch[1] was able to investigate the gonad of an hermaphrodite which had been removed through an operation and which showed itself clearly to be an ovotestis. The individual possessed female extra-genitals, but the clitoris was quite enlarged with the opening of the urethra ventral on it. The vagina ended blindly and there was no uterus. The hair covering of the body was female. Mammary glands were missing and the larynx was male. The individual had always considered herself to be female but had never menstruated nor had any libido. The operated gland was a degenerate testis which bore a small tubercle with ovarian character.

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[1] Goldschmidt, R., "Die biologischen Grundlagen der Intersexualität und des Hermaphroditismus beim Menschen." Arch. Rassen u. Gesellsch. Biol., 12, 1916.

[2] Steinach und Lichtenstein, Umstimmung der Homosexualität durch Austausch der Pubertätsdrüsen." Munich Med. Wochenschr., 21, 1918.

[3] Fischer, E., "Die Rehobother Bastards." Jena, 1913.

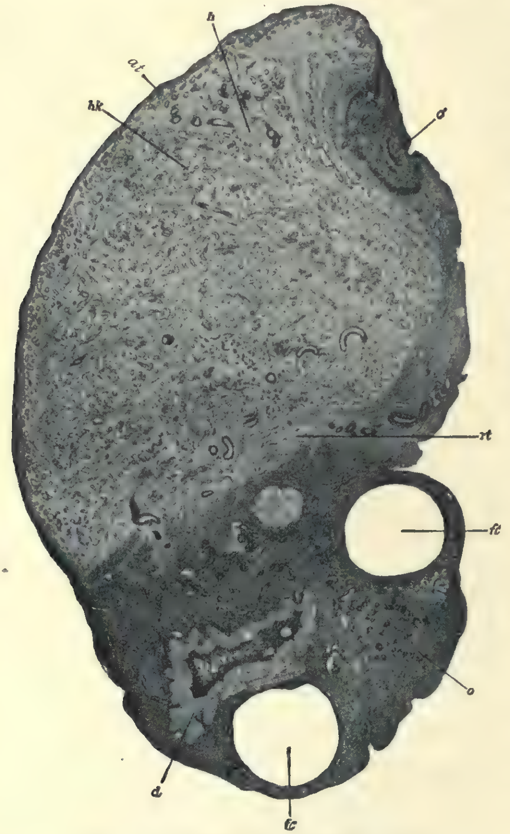

FIG. 113.—Ovotestis of the case Salén.

o, o^1, ovarial part; h, testicular part; at, albuginea testis; hk, testis canals; rt, rete testis; fc, follicle cysts; cl, corpus luteum.

After Pick.

A very similar example was the case Salén described by Pick.[2] A section through the ovotestis of this hermaphrodite is given in Fig. 113. The biological interpretation of this kind of hermaphroditism is extraordinarily difficult, since for both man and the other Mammalia there is no comparable experimental material.

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[1] Gudernatsch, J. E., "Hermaphroditismus verus in Man." Amer. J. Anat., 11, 1911.

[2] Pick, L., "Über den wahren Hermaphroditismus des Menschen." Arch. mikr. An., 84, 1914.

It is worthy of note that taken altogether these cases bear a considerable resemblance to the features described by Lillie and others for the freemartin. The "hermaphrodite" could well be therefore an analogous case of extreme hormonic intersexuality on a female basis. It is not to be denied, however, that the converse is conceivable, that is, male constitution with a secondary intersexual shifting towards the female side. A detailed discussion seems aimless so long as it has not been possible to produce experimentally in the Mammalia the higher stages of intersexuality by experimenting on embryos.

An important case of a rather different type has been studied by Simon.[1] The individual is described as possessing male instincts, including erotic instincts, female breasts, menstruation, female pubic hair boundary, rudimentary penis, oviducts, and an orifice (it is unknown whether it was urethra or canalis urinogenitalis). The operation showed in the right inguinal canal an oviduct with ostium, ligamentum latum, and parovarium; furthermore, a gonad with epididymis and vas deferens. Microscopically the gonad comprised both ovary and testis parts. This case looks more like gynandromorphism.

E. The Sex Ratio

The statistical material regarding the conditions of the sex ratio in man is quite extraordinary. Corresponding to its extent it is always being drawn upon to support this or that sex theory, and thereby the most remarkable things have been promulgated, the details of which it would serve no purpose to discuss. A famous astronomer, for example, has demonstrated mathematically from statistics that the father has nothing at all to do with the determination of the sex, only the mother, and that the sex is not fixed at a definite moment but is the result of a whole series of accidental causes, which now work this way, now in that direction—he compares it with the water particles in a dividing stream.[2] All our foregoing discussion leaves it superfluous to discuss this point any further. We can simply refer the reader to what was said on a previous page in connection with the ratios of the sexes in other animals.

---

[1] Simon, W., "Hermaphroditismus verus." Virchow's Archiv., 172, 1903.

[2] Newcomb, S., "A Statistical Inquiry into the Probability of Causes of the Production of Sex in Human Offspring." Carnegie Inst. Publ., 1904.

And for man, just as we saw for the lower animals, a series of causes are conceivable which could be responsible for the variation from the norm 1 : 1 sex ratio.

The first possibility is again the selective elimination of one sex and this has also been demonstrated here. The ratios of the sexes according to census statistics are given by Bälz[1] as follows :—

Number of ♀ : 100 ♂

Great Britain	107·0	Belgium	101·5
Norway	106·4	Italy	101·0
Denmark	105·8	Poland	99·5
Sweden	104·9	Greece	98·6
Spain	104·9	Japan	98·0
Austria	103·5	India	96·0
Germany	103·2	Bulgaria	95·8
European Russia	102·9	Serbia	94·3
Switzerland	102·9	Siberia	94·3
Hungary	102·4	Caucasus	90·1
France	102·2	Korea	88 5
Holland	101·7	Russian Central Asia	85·1
Ireland	101·6	China	80·1

It will be seen that as a rule an excess of females is present. Where there is an excess of males one has every reason to doubt the statistics. Compare this table with the statistics of the births, and one finds that almost always the male births are in excess, on an average the ratio being 106 : 100. For example :—

♂ : 100 ♀

Germany	105·2	Spain	108.3
England	103·6	Austria	105·8
France	104·6	Hungary	105·0
Italy	105·8	Switzerland	104·5
Russia	105·4		

More boys are therefore born, but they are eliminated in early childhood. Indeed the elimination begins to take place before birth, for the statistics of still-born children indicate a still greater excess of boys, namely :—

Germany	128.3
Austria	132·1
France	142·2
Italy	131·1

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[1] E. von Bälz, "Die Verhaltniszahl der Geburten in verschiedenen Ländern," Korrespondenzbl. deutsch. Anthr. Ges., 42, 1911.

Finally, in the investigation of aborted embryos a still greater boy excess is found, namely, 160 ♂ : 100 ♀.[1] Thus there can be no doubt of a selective elimination of the male sex. But these statistics supply no answer to the question whether the relation of the fertilized eggs is 1 : 1 or not, and why it varies from this norm. A safe answer regarding this is scarcely attainable.

Other possibilities of influencing the sex ratios are the same as those already given when discussing the Mammals, and reference should be made to the previous discussion on differential fertilization, which can be brought about by the egg or by the sperm. For some of the possibilities treated on p. 232 there are statistical parallels for man. Statements were mentioned pointing out that hybridization influenced the sex ratio, and it was regarded as a special case of the selective elimination of a sex. For man Pearl's reports may be compared with this. He gives the sex ratio in Argentine for pure Italian marriages 100·77 ♂ : 100 ♀, for Argentinos 103·26 ♂ : 100 ♀, and for the mixed cross 105·72 ♂ : 100 ♀. On the other hand, E. Fischer finds[2] for the much more different cross Boers-Hottentots 107·6 : 100 in comparison with 108·6 for the Boers.

For the possibility of a differential fertilization ability by the two sorts of sperms statements were adduced relating to the modification of the sex ratio according to the season and the age of the mother. Here also information is available regarding man. Duesing, as well as Heape,[3] finds more boy births in winter, and believes that the smallest number of boys coincides with the time of greatest fertility, namely :—

	Duesing for Prussia.	*Heape for Cuba*	
♂ : 100 ♀.		*White.*	*Coloured.*
Time of highest birth rate.	105·92	104·29	99·3
„ „ lowest „ „	108·77	108·02	108·3

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[1] Lenhossek, M. von, "Das problem der Geschlechts-bestimmenden Ursachen." Jena, 1903.—Duesing, K., "Die Regulierung der Geschlechtsverhältnisse bei der Vermehrung der Menschen, Tiere und Pflanzen." Jenaische Ztschr., 17, 1884.

[2] l.c. ; see also the material in K. Pearson, "The Chances of Death." London, 1897.

[3] Bidder, F., "Über den Einfluss des Alters der Mütter auf das Geschlecht des Kindes." Ztschr. Geburtsh. Gynäk, 11, 1878.—Geissler, A., "Beiträge zur Frage des Geschlechtsverhältnisses der Geborenen." Ztschr. sächs, statist. Bur. Dresden, 35, 1889.—Punnett, B. C., "On Nutrition and Sex Determination in Man." Proc. Camb. Phil. Soc., 12, 1903.—Heape, "The Proportion of Sexes Produced," etc. Phil. Trans. R.S. London, B. 200, 1908.—Pearl, R., "On the Relation of Race-Crossing to the Sex-Ratio." Biol. Bull., 15, 1908.

There might, therefore, be a periodicity here. So far as the age of the mother is concerned Bidder finds the ratio 122·2 ♂ : 100 ♀ for mothers under nineteen, for mothers of twenty to thirty years 104·6 ♂ : 100 ♀, and for mothers over forty years 131 ♂ : 100 ♀. Analogous figures have been given by Geissler for the ratios in large and small families, namely, 106·8 ♂ : 100 ♀ for families with over seven children and 105·8 ♂ : 100 ♀ for smaller families. Punnett, however, could not confirm this.

Finally, there is the possibility of a different fertilization ability of freshly expelled and old eggs, as was mentioned in connection with Thury's work. A well-known old midwife's superstition states that the time of conception (in regard to menstruation) has an influence on sex. Siegel has recently communicated statistics which are again supposed to demonstrate that conception in the first week after menstruation tends to give a marked excess of boys, whilst if in the third week a marked excess of girls results. For explanation, however, he brings forward Hertwig's case of over-ripeness in amphibia, an attempt which (apart from the paucity of the statistical material) must arouse misgivings owing to the fact that the time relation between menstruation and ovulation[1] is still a matter of uncertainty.

There is no point in adding to the number of these citations. They afford us no insight into the causes of "abnormal" sex ratios. What these causes may be has been discussed from a theoretical point of view on an earlier page. The list of possibilities given there provides also an answer to the question —"What prospects are there, theoretically, for a voluntary control of the sex ratio?"

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[1] Siegel, "Münch. Med. Wochenschr.," 1916.—Novak, V., "Die Beziehungen Zwischen Ovulation und Menstruation," etc. Biol. Centralb., 41, 1921.

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